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OSTEOPOROSIS AND OSTEOPENIA MANAGEMENT IN WOMEN: SURVEY, CASE-REFERENT STUDY, AND INTERVENTIONAL EXERCISE TRIAL

A Dissertation
Submitted to the Graduate Faculty of the
Louisiana State University and
Agriculture and Mechanical College
in partial fulfillment of the
requirements for the degree of
Doctor of Philosophy

in

The School of Human Ecology

by
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August 2005

I would like to humbly dedicate my work to my family who has been of a major emotional, financial, and moral support to me during these four years while working on my PhD. Life has taught me that I could be betrayed by any person on earth, with the exception of my family... I dearly appreciate their unconditional love.

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ABSTRACT

Three studies are presented; the first epidemiological study was a survey of Baton Rouge/New Orleans physicians who manage osteoporosis. When the respondents' answers were compared to selected guidelines, they displayed poor knowledge regarding osteoporosis prevention, diagnosis, and treatment ($X^2=39.88$; $P<0.0001$). Rheumatologists and endocrinologists scored globally better on osteoporosis management when compared to ObGyn ($OR= 6.98$) ($CI=2.4$; 22.8). Physicians with more years of experience were more knowledgeable of osteoporosis care ($OR=1.04$) ($CI=1.014$; 1.071).

The second epidemiological study was a case referent study looking at osteoporosis treatment and patient adherence of selected women in Baton Rouge. Results showed that osteoporosis management depended partly on patient adherence. Barriers to patient's adherence varied from physiological to psychological reasons. Physicians need to provide more explanation and motivation to the patients. Spine was the area most affected and showed more improvement with treatment than the femur ($P<0.01$). Bisphosphonates were the most effective treatment for the spine ($P<0.05$). In patients with osteoporosis, being on just calcium and exercise is not enough to counteract bone resorption. They also need to be on an anti-resorptive therapy. Low body mass index, genetics, and history of fractures were negatively correlated to bone mineral density (BMD) increase ($P<0.05$).

The third interventional pilot study was a non-randomized controlled study done on osteopenic postmenopausal women to examine the effect of calcium supplements and core/lower back strengthening exercises on lumbar density and muscle strength. Repeated measures analysis showed that both groups increased in isometric lumbar strength with time ($P=0.02$). When fosamax and exercise were taken as treatments, with baseline BMD as a covariable, the

one-tailed P value of the two-way ANOVA showed a numerically positive but not significant increase in the exercise group (yearly change= 2.373 ± 2.625 ; T value=0.9; P=0.21). Also, the exercise group showed increased feelings of well-being as opposed to the control group who showed no change or worsening. One woman in the control group fractured a bone. Ultimately, osteoporosis management relies on physicians' knowledge, involvement, and patient adherence. Calcium, exercise and anti-resorptive treatments are needed in case of osteoporosis. Calcium supplements and site-specific strengthening exercises may be enough in case of osteopenia.

CHAPTER I INTRODUCTION

According to the National Institute of Health (NIH), “osteoporosis is defined as a skeletal disorder characterized by compromised bone strength” predisposing a person to an elevated fracture risk (NIH, 2001). It has been estimated that osteoporosis affects approximately 25 million people in the United States, and most are women (McCoy, 2001). An average of one million Americans suffer from fractures per year and the total estimate cost is over 14 billion dollars according to Riggs et al., (1998) and is about \$17 billion annually according to the National Osteoporosis Foundation (NOF, 2002). Albeit osteoporosis is both “preventable and treatable” (Eastell, 1998), yet, according to McCoy (2001) it is often “undiagnosed and untreated”. Because the number of treatment options is escalating, the decision-making process is becoming a hard task. There is even some controversy regarding the active treatment of osteoporosis (Speroff, 1999). Moreover, there has been no general consensus with respect to the exact type and amount of exercise that would be beneficial to patients with osteoporosis (Watts NB, 1994; Henderson et al., 1998).

This dissertation starts by a literature review of osteoporosis (Chapter II). The definitions and the different types of this disease are presented at first. The review then gives a brief overview about the pathogenesis, prevalence of osteoporosis, the risks associated, as well as the management procedures currently applied. Then, it presents the conflicting results of the previous research that had studied the relationship between osteoporosis and physical activity, osteoporosis and muscle strength in postmenopausal women. The studies are summarized and presented according to their design, i.e. randomized controlled trials, non-randomized controlled trials, and descriptive studies. An analysis of the disparities in the literature will accrue, along

with comparison with other studies in the literature as well as two other meta-analyses. The review concludes with exercise guidelines, summary and future studies' suggestions.

The problem of low bone mineral density (BMD) in postmenopausal women in Baton Rouge is addressed by a three-pronged approach: two epidemiological studies (Chapters III and IV) and one interventional study (Chapter V).

Chapter III is a survey about physicians who manage osteoporosis in Baton Rouge and New Orleans areas. The purpose of the survey is to collect descriptive information on how physicians who treat osteoporosis in Baton Rouge/New Orleans communities diagnose, prevent, treat, and follow up with osteoporosis patients, and how the physicians' recommendations compare with standards World Health Organization (WHO) and National Osteoporosis Foundation (NOF) according to their area of specialty and their years of experience.

Chapter IV is a case-referent study. The goal of this study is to investigate the types of interventions for osteopenia/osteoporosis offered to a population-based case-referent of postmenopausal women with osteopenia/osteoporosis, and then to look at the outcome of these methods, including patient adherence to the treatment protocol. The objectives were to answer the following questions: 1) Based on the treatment followed, what kind of response is seen on the patients upon the second/third year of treatment? What is the best treatment for osteoporosis in practice? 2) Are patients compliant with the physician's prescribed treatment? If not, what are the barriers to compliance? 3) Does optimal osteoporosis management lie exclusively on patient adherence?

Chapter V is a pilot non-randomized controlled trial. The goal of the study is to design an appropriate, convenient, and cheap home exercise program for postmenopausal women suffering from low bone density (osteopenia) in the lower back. The program consists of site-

specific core/lower back strengthening exercises. The primary objective is to prevent the accelerated bone loss induced by menopause via the core/lumbar strength exercises. Secondary objectives are to improve isometric lumbar strength and overall quality of life.

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CHAPTER II LITERATURE REVIEW

2.1. Definitions

Osteoporosis can be broken down into two words; the term “osteo” means bone and the term “porosis” means porous or having pores. Osteoporosis refers to a disease causing the bone structure to become more open and porous resulting in fractures. According to National Institute of Health (NIH), osteoporosis is defined as “a skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk fracture; bone strength reflects the integration of two main features: bone density and bone quality” (NIH Consensus Development Panel, 2001). Bone strength primarily implies the combination of bone density and bone quality. Bone density is expressed as grams of mineral per surface (g/cm^2) or volume (g/cm^3). Bone quality refers to the integrity, remodeling, architecture, and geometry of the bone. Currently, there is no accurate measure of global bone strength. Bone mineral density (BMD) is often used as an estimate measure for bone strength while it only accounts for 70% of bone strength. The World Health Organization (WHO) operationally defines osteoporosis as “bone density 2.5 S.Ds below the mean for the young white adult women”. The WHO definition of osteoporosis was established for Caucasian women, because of paucity of data for other population groups (Sanborn and Simmonds, 2002). The term osteopenia is a less advanced stage of bone loss as compared to osteoporosis; it reflects BMD values “between 1 and 2.5 standard deviations below the mean of young adults of the same race and sex”(Khan et al., 2002). BMD results are represented as T-scores and Z-scores. The main difference between the two scores is the age variable, where the T uses the mean value of young adults of the same gender as a reference and the Z score uses the mean value of the people of the same age and gender. Z-score is a more appropriate measure for children and young adults, who haven’t yet achieved their peak bone

mass (PBM). However, the reference “young adults” population used in the T score is assumed to represent a standard PBM (Gourlay and Brown, 2004). Each standard deviation reflects a 10- to 12% difference in BMD (McGarry et al., 2003) and each 1 SD decrease in BMD reflects a doubling of fracture risk (NIH, 2001). Regardless of the BMD scores, a patient with history of fractures is considered to have severe osteoporosis (Lane et al., 2003).

Strength exercise refers to the type of exercise designed to increase the ability of the muscle to move and perform functions of daily activity such as lifting, carrying, pushing, pulling, sitting, standing, walking, and climbing stairs. Strength exercise can be performed with weights (progressive resistance training; isokinetic resistance training) or without weights (isometric strength training). “The gain in strength can be either static (isometric) in which no observable changes occur in muscle fiber length, or dynamic in which the muscle action produces movement of the skeleton” (ACSM’s guidelines, 2000).

Muscle strength refers to “the maximal force (properly expressed in Newtons, or Kg) that can be generated by a specific muscle or muscle group at a given velocity”. Static or isometric strength can be measured conveniently using different instruments, such as cable tensiometers and handgrip dynamometers. “Dynamic strength can also be measured using the direct 1-repetition maximum test (1-RM), the heaviest weight that can be lifted only once using good form” (ACSM’s guidelines, 2000).

2.2. Types of Osteoporosis

Although bones might appear as non-living materials due to their rigid structure, they are actually made of 5% of living materials. Osteoblasts (bone building cells) and osteoclasts (bone scavenger cells) are the two major types of cells that form the bone living material. Bearing this

information in mind, it becomes important to differentiate between the two types of osteoporosis, primary and secondary.

There are two types of primary osteoporosis: Type I and type II. Type I occurs only in women due to decreased estrogen and increased osteoclast activity, typically in the years following menopause, from age 50 to 70. Type II most commonly affects men and women over the age of 75 due to decreased osteoblast activity and decreased bone formation (Gruver, 2004).

Secondary osteoporosis, as its name indicates, it is secondary to other underlying diseases, we will state but a few: secondary hyperparathyroidism, diabetes, glucocorticoids intake, excessive thyroid hormone therapy, hypogonadism, hypoestrogenemia, and tamoxifen (Shephard, 2002; McGarry et al., 2003).

2.3. Pathogenesis

Bone is a living tissue, and the cells in the bones are constantly changing. They go through a remodeling cycle that starts with bone resorption by osteoclasts, followed by bone formation by osteoblasts. Bones increase in length up till about 20 years of age and keep on increasing in mass up till about 30 years of age. This is why an adequate intake of calcium during growth is needed to achieve adequate bone mineralization. Peak bone mass is a chronic effect and is attained at 30 years of age. Therefore, bones can be compared to a saving account: the more we store calcium in them, the higher the peak bone mass will be at 30 to 35 years old, and the higher the prevention against risk fractures will be for later years (Shils et al., 1998). After 30 years of age, bone resorption exceeds bone formation, and this negative calcium balance is accentuated in postmenopausal women who stop secreting estrogen, leading to a decrease in calcium absorption and an increased osteoclast activity (Hughes et al., 1996). The trabecular

bone found mainly in the vertebrae has a larger surface area and remodels more rapidly than the cortical bone, which makes it more susceptible to osteoporosis (Kenny et al., 2003).

2.4. Prevalence

Osteoporosis is considered one of the most common skeletal disorders in elderly. The bone loss process can occur with no symptoms and the individual feels fine until a fracture occurs; therefore the attribute “silent” given to the disease. If untreated, it can lead to suffering, dysfunction, and death in the elderly population (Goldmann and Horowitz, 2000). An estimate of 44 million Americans is affected by the bone loss. More specifically, 34 million suffer from osteopenia (low bone mass) and 10 million have osteoporosis (Kenny et al. 2003). More than 47 million are expected to have low bone mass by the year 2020 (NOF, 2004).

2.5. Risks and Costs Associated

According to the investigators of the National Osteoporosis Risk Assessment trial (NORA), women suffering from osteoporosis have a relative risk of sustaining a fracture that is four times that of women free from the disease; as for women with osteopenia, their relative risk doubled (Siris et al., 2001). Fractures occurring as a result of osteoporosis constitute a serious and escalating threat to our aging population (Melton, 2000). These threats vary from diminished quality of life to its complete loss (Hertel and Trahiotis, 2001). Estimates of one out of two women and one out of eight men have an osteoporosis-related fracture in their lifetime (Gruver, 2004). In the United States, over half a million of women suffer from vertebral fractures, over ¼ million women suffer from hip fractures, and another ¼ million men suffer from osteoporotic fractures each year. The total estimated cost of the one million Americans suffering from fractures is over 14 billion dollars according to Riggs et al., (1998) and is about \$17 billion

annually according to the National Osteoporosis Foundation (NOF press release, 2002). Although less prevalent than vertebral fracture, hip fracture is the predominant cause of death and accounts for the major share of the medical cost (Melton, 2000). According to the NIH, (NIH, 1992), patients die within six months of hip fractures in 12 to 20% of the cases, but since the population at risk of osteoporosis is enormous, the potential cost of preventing those fractures is also high. Consequently, there is continuous argument about the relative cost-effectiveness of various management strategies (Melton, 1999), albeit the social benefit and the cost efficiency in treating these high-risk individuals seem to be very clear (Cuddihy et al., 2002). Although osteoporosis can be prevented and treated, its efficient management is still underutilized among postmenopausal women who experience a fracture (McCoy, 2001; Cuddihy et al. 2002). A myriad of variables affecting bone, balance, and muscle strength will in turn affect fracture risk (Rutherford, 1999). Age is a great example; in fact, given the same bone density, fracture risks increase from 8- to 10-fold from age <45 years to >80 years (Hui et al., 1988). Knowing that the most common cause of hip fractures is falling (Cummings et al., 1995), it is more useful to engage the elderly in safe physical activities that would strengthen their muscles and reduce falling than increasing their bone mineral density per se (Shephard, 2002).

2.6. Prevention

The prevention starts as early as childhood because calcium is needed during childhood through adulthood until the peak bone mass is reached. The first 30 years of a person act like they are storing calcium like a reservoir; the more calcium stored, the less the likelihood of a later fracture. A plethora of lifestyle interventions can be very beneficial to osteoporosis prevention such as the following:

-Having a healthy and varied diet with adequate calcium and vitamin D daily intake: Common sources of calcium are milk and dairy products. Common food sources of vitamin D are egg yolk, fatty fish, and cod liver oil. While an intake of 1000-1500 mg calcium is recommended daily, it is still deficient among more than 90% of the women and more than 50% of the men in the United States. Similarly, while an intake of 400 to 800 IU of vitamin D is recommended daily, its deficiency is prevalent, resulting in poor calcium absorption, increased bone loss, and decreased mineralization elderly (Gruver, 2004).

-Leading an active lifestyle: Growing evidence suggests that weight bearing, resistance and strength exercises stimulate bone growth and muscle strength (Silverwood, 2003) and improve balance.

-Cutting down on smoking: Smoking affects the bone negatively by lowering the estrogen levels in the blood (Papazian, 1991) and it has shown to increase the risk of hip fracture in the aging population (Silverwood, 2003).

-Controlling alcohol intake: Excessive consumption of alcohol (>2cups/day) suppresses calcium absorption (Papazian, 1991) and increases the risk of falls.

-Controlling caffeine intake: It is speculated that excess caffeine consumption increases urinary excretion of calcium as well as rates of bone loss. Results are still controversial. Patients who consume a lot of caffeinated beverages are advised to have an adequate intake of calcium to counterbalance the urinary calcium loss (Follin and Hansen, 2003).

-Avoiding excessive weight loss: Thin women [Body Mass Index (BMI) <18.5] are at higher risk because they lose muscle mass, become susceptible to falling and are less able to sustain the impact of falls.

- Exposing the body to sunrays: This would encourage the synthesis of vitamin D precursors by the skin via exposure to UV light.
- Being aware of the risk factors of osteoporosis: Turner et al. (2003) has shown that an osteoporosis prevention program for a group of middle-aged women may help promote osteoporosis prevention behaviors.
- Undergoing a therapy if needed, either anti-resorptive therapy (bisphosphonates, estrogen, calcitonin, Selective Estrogen Receptor Modulator SERM) or bone formation therapy (Parathyroid Hormone –PTH- such as Forteo).

2.7. Diagnosis

Diagnosis of osteoporosis should include a thorough medical history identifying the risk factors for low bone density among other tests such as a physical examination for any indications of fractures, a bone mineral density (BMD) testing, and a routine lab tests to rule out secondary causes (Follin and Hansen, 2003). Risk factors are the ones that increase the likelihood of developing osteoporosis. The risk of osteoporosis is determined by the amount of calcium deposited during adulthood and by the loss rate of the bone mass. According to the National Osteoporosis Foundation (NOF) Guidelines, the following risk factors have been identified:

- Advanced age: The aging process leads to loss of muscle mass, deficit in estrogen, and weakening of the bones.
- Gender: The risk of developing osteoporosis is greater for women than for men. An estimate of one-third of postmenopausal women will undergo an osteoporotic fracture in their lifetime (Melton, 2000). In fact, women are at a greater risk of osteoporosis than men because they have a smaller body size, they have less bone, they are thinner, they have less muscle mass, and they lose bone more rapidly because of the hormonal changes during menopause. Postmenopausal

estrogen deficiency is the chief culprit for osteoporosis in women because estrogen enhances calcium absorption and has an anti-resorptive effect on bones.

-Race: Race and gender play an important role in the prevalence of osteoporosis and the incidence of fracture. White (Caucasian and Asian) postmenopausal women have the highest age-adjusted fracture incidence. Nevertheless, African American women, Hispanic women, men, and children are also at a significant risk of fracture. Among men, white men appear to be at greater risk. These differences are mainly due to discrepancies in peak bone mass and rate of bone loss. Other reasons are greater total body potassium and thus higher muscle mass (Pollitzer and Anderson, 1989), as well as differences in bone geometry.

-Bone structure and body weight: Women with a small frame size and low BMI (<18.5) have less muscle mass and tend to have weaker bones; thus they are more prone to develop the disease.

-History of bone fractures: Previous fractures are an indication of low bone mass.

-Family history of osteoporosis (heredity): Young women whose mothers have osteoporosis are at a greater risk of developing the disease. Genetic factors relating to bone mass acquisition, bone remodeling, or bone structure are also being identified.

-Menopause/Menstrual history: Having menopause at an early age because of either surgery or natural reasons increases the risk of developing osteoporosis because of lack of estrogen at an early age. Moreover, women who stop menstruating before menopause because of excessive exercise or disordered eating may also lose bone tissue and develop osteoporosis (female athletic triad).

- Hypogonadism: it is defined as “low production of the male sex hormone testosterone”, and it increases the risk of developing osteoporosis in men. In fact, sex steroids secreted during puberty increase peak bone mass and bone mineral density.
- Removal of ovaries: Estrogen production stops after removal of the ovaries.
- Lifestyle: Excessive alcohol, caffeine, and tobacco use, low intake in calcium and vitamin D, and lack of exercise are all factors that are negatively correlated to bone health.
- High Phytate, high oxalate, high protein, and high sodium: Phytate (in whole wheat bran) and oxalate (in spinach and rhubarb) inhibit calcium absorption; high protein or high sodium intake increase urinary calcium excretion.
- Certain medications: Prolonged usage of steroids to treat asthma or arthritis, anticonvulsants, certain cancer treatments and aluminum-containing antacids interfere with calcium homeostasis or absorption.
- Certain diseases: Cystic fibrosis, celiac disease, and inflammatory bowel disease lead to secondary osteoporosis by inhibiting calcium absorption among other nutrients. Also, hyperthyroidism and hyperparathyroidism increase the rate bone resorption and lead to osteoporosis.

2.7.1. Guidelines for Bone Mineral Density Testing

The NOF has established guidelines for BMD testing in postmenopausal women that can be useful for physicians to identify candidates for screening. According to NOF, all postmenopausal women who are less than 65 years of age with one or more additional osteoporosis risk factors, all women above 65 years of age, all postmenopausal women who sustain a fracture, all women considering osteoporosis therapy, and all women who have been on hormone replacement therapy (HRT) for a minimum of 1 year are advised to take a BMD test.

2.8. Treatment

2.8.1. Patient Beliefs and Medication Use

Cline and coworkers (2005) developed a health belief model associated with the decision of using a newer antiresorptive therapy (bisphosphonates and calcitonin) as compared to no prescription therapy. They found in their cross sectional survey on 983 postmenopausal women that constructs such as “perceived susceptibility to the disease”, “perceived benefits and barriers to the use of antiresorptive” treatment, and BMD screening were all associated with the use of antiresorptive therapy. These results were concordant with other prospective studies that showed that previous knowledge of low bone mass was positively correlated to the positive changes in exercise habits and to the increase in calcium and vitamin D supplements (Jamal et al., 1999). In a similar vein, Hsieh and Turner (2001) reported that women who showed more concern about osteoporosis were more likely to commit to treatments such as hormone therapy, weight-bearing exercise, or calcium and vitamin D supplements. Congruent with these results, Blalock and colleagues showed that women who expressed fewer barriers and more benefits to exercise were more likely to engage in weight-bearing exercises (1996). These findings highlight the importance of the dissemination of osteoporosis management knowledge to both physicians and patients.

2.8.2. Nutrition

Osteoporosis is a multi-factorial disease. There is a plethora of factors that affect the risk of osteoporosis, such as age, sex, race, exercise, diet, stature, and hormonal status; among these factors, only nutrition and exercise can be manipulated by the individual (Kuntze et al., 1989). The chief nutrients affecting the bone are calcium and vitamin D.

2.8.2.1. Calcium and Vitamin D

Bone is a connective tissue. It is composed of (5%) living materials (lining cells, osteocytes, osteoblasts, osteoclasts) and of (95%) non-living materials (protein matrix encrypted with minerals, which give the mechanical functions of the bones, such as stiffness; rigidity; resilience). The non-living material is formed of 50% protein and 50% minerals. Among the proteins, 90% is collagen and 10% is non-collagen, such as osteocalcin. Among the minerals, around 55% is phosphorus, 40% is calcium, and 5% is carbonate and other trace minerals (Shils et al., 1998). A simple algebra of the numbers above suggests that 19% of the bone tissue is made of calcium. Knowing that the total body calcium is around 0.9 to 1.5 Kg, 99% of body calcium is in the skeleton.

During adult life, bone grows in length and keeps on growing in mass until 30 to 35 years of age. Dietary calcium needs to be adequate during this critical period (10-35 years of age) to attain a high PBM. The RDA of calcium is 1000-1500 mg; the higher range is recommended for elderly and post-menopausal women. Adequate calcium intake is considered standard care for all postmenopausal women, either alone or in combination with other pharmacological treatments (McGarry et al., 2003). Food sources of calcium are milk and dairy products, sardines, broccoli, nuts, fortified beverages (orange juice), and sesame seeds. Calcium supplements are available in the form of calcium carbonate and calcium citrate. The latter is better absorbed than calcium carbonate in the body (Lin and Lane, 2004).

Vitamin D maintains serum calcium and phosphorus homeostasis by stimulating their absorption from the gut; thus vitamin D, taken with calcium, slows bone loss in postmenopausal women. The RDA of vitamin D is 400-800 IU. Sources of vitamin D include egg yolk, liver,

fatty fish, cod liver oil, and fortified milk and dairy products and skin production of vitamin D with sun exposure.

Literature has shown that supplements of calcium and vitamin D combined decrease the risk of non-vertebral fractures and increase the total-body BMD in elderly men and women with no osteoporosis (Dawson-Hughes et al., 1997).

While Wymelenberg (among other researchers) recommended in the Harvard Health Letter in 1994 that women suspecting to have menopause should increase their calcium intake up to 1500 mg daily owing to the upcoming decrease in estrogen production and the subsequent decrease in calcium absorption, Cumming and coworkers (1997), on the other hand, argued against this high calcium intake. They thought that daily calcium recommended intakes of 1-1.5g would accentuate rather than attenuate fracture risk. Excess calcium may suppress PTH secretion and thus hamper the natural bone turnover.

2.8.2.2. Calcium and Exercise

Research on calcium effects in interaction with exercise on the bone has been controversial. This conflict may arise from the fact that calcium may be essential to skeletal integrity but may not be enough to prevent osteoporosis on its own (Heaney, 1987). In a critical review of the literature, Specker (1996) concluded that exercise can only be beneficial to bone density if complemented with a minimum calcium intake of 1000 mg; moreover, calcium supplements can only be beneficial to bone health if complemented with adequate physical activity. In fact, several researchers have argued that calcium is crucial for bone development; yet, its intake alone cannot suppress bone loss and replace a disintegrating matrix (Kreiger et al., 1992). Congruent with this argument, Heaney (1992) mentioned that calcium should be viewed

as a nutrient and not as a drug per se; thus, its supplementation will be useful to alleviate calcium deficiency.

2.8.2.3. Other Nutrients

While an excess of nutrients such as sodium, caffeine, phosphorus, or protein potentially affect bone mineral through increased calcium excretion, phytoestrogens in soy foods may attenuate bone loss through estrogen like activity (Lewis and Modlesky, 1998).

2.8.3. Pharmacologic

Osteoporosis reversal can be achieved by either decreasing bone turnover (anti-resorption), and/or increasing bone mass formation (anabolism) (WHO guidelines, 1994). All the following treatments listed below have been approved by the US Food and Drug Administration (FDA).

2.8.3.1. Anti-resorptive

Anti-resorptive drugs are those that decrease resorption of the bones, such as estrogen, bisphosphonates, and calcitonin. These drugs decrease the rate of bone formation as well. The only difference is that this last happens in a few months, whereas the decrease in bone resorption happens within weeks. Thus the ultimate result is that the decreased resorption is larger than the decreased formation, leading to a net increase in bone. Yet, it takes two to three years for the bone density to change (Eastell, 1998).

2.8.3.1.1. Estrogen

Estrogen used for the alleviation of postmenopausal symptoms did receive approval from FDA in 1988 as a treatment for osteoporosis. It has been shown that its usage decreases the odds of hip fracture by 4% if taken alone and by 11% if taken with progestin (Michaelsson, 1998); yet, a positive correlation has been shown between estrogen use and breast cancer and

endometrial cancer. Adding progestin to it may lower the risk of uterine cancer, but also increase a woman's risk of developing breast cancer (Papazian, 1991). Once estrogen therapy is stopped, it is followed by rapid bone loss (Speroff, 1999); thus, other treatments need to be implemented to counteract this effect. Some women might not respond to hormone therapy and the reason is unknown. Some theories can be ruled out such as compliance, calcium and vitamin D deficiency, renal and hepatic problems, eating disorders, high intake of alcohol, and smoking (Papazian, 1991). A recent review in the literature has highlighted that estrogen was not recommended for osteoporosis treatment because the health risks outweighed the benefits (Lin and Lane, 2004). According to the Women's Health Initiative Writing Group, although there were 5 fewer hip fractures per 10,000 person years in persons taking conjugated equine estrogens plus progestin, the number of each of coronary heart disease events, strokes, pulmonary embolisms, and invasive breast cancers increased by 7; 8; 8; and 8 respectively (Rossouw et al., 2002). On another note, Minelli et al. (2004) have shown that women with no menopausal symptoms were at increased risk of breast cancer from (HRT) use. Thus, even for women with menopausal symptoms, a tailored individual-based approach would be more adequate than a population-based approach for decision-making.

2.8.3.1.2. Bisphosphonates

Interestingly, hormones and drugs affect different regions in the body with different magnitude (Eastell, 1998); for prevention and treatment of osteoporosis, bisphosphonates are the most potent and effective class of drugs. They act by inhibiting osteoclast activity (Lin and Lane, 2004). Alendronate (Fosamax), risedronate (Actonel), and etidronate (Didronel), are all compounds of the bisphosphonates family (Papazian, 1991). However, the first 2 are the most popular and they are known to decrease hip and vertebral fractures (Lin and Lane, 2004).

Alendronate administration was shown to increase bone density in both the spine and the hip in women who already have osteoporosis (Speroff, 1999);

Similarly, Harris et al. (1999) showed in a randomized controlled trial that risedronate administration to women with osteoporosis reduced new vertebral fractures by 65% after 1 year and by 41% after 3 years; and non-vertebral fractures by 40% in 3 years. Moreover, it significantly increased BMD at the lumbar spine (4.3%), femoral neck (2.8%) and trochanter (4%).

Etidronate is a non-hormonal drug, proven to slow down the process of bone resorption in the spine (Papazian, 1991).

Adverse effects were reported upon the oral intake of bisphosphonates such as abdominal pain, GI inflammation, and ulcers. To circumvent this problem, patients have to remain upright for the first 30 minutes after the ingestion of the medication.

2.8.3.1.3. Selective Estrogen Receptor Modulators (SERMS)

Raloxifene (EVISTA) and Tamoxifen are selective estrogen receptor modulators. They both appear to have an oestrogenic activity on the bone. Both appear to be protective against breast cancer (WHO guidelines). Raloxifene works by binding to estrogen receptors and works as an estrogen agonist on bone (anti-resorption), lipids (deep vein thrombosis), and blood clotting (pulmonary embolism), and as an estrogen antagonist on the breast (cancer risk) and uterus. Studies have shown a decrease in vertebral fractures of 68%, 46%, and 41% at 1, 2 and 3 years respectively upon daily ingestion of 60 mg raloxifene. However, there was no hips' fracture protection (Maricic et al., 2002). Yet, Raloxifene (EVISTA)'s effect on the increase on BMD is slightly less than that seen with Alendronate (Speroff, 1999);

2.8.3.1.4. Calcitonin

The effects of calcitonin are better documented on the spine and the forearm rather than the hip in women with osteoporosis in a dose-dependent manner (WHO guidelines). In a 5-years randomized controlled trial, a 200 IU daily intake of calcitonin was shown to increase lumbar BMD (1-1.5%) and to decrease new vertebral fractures by 33% when compared with placebo (Chestnut et al., 2000); nevertheless, no hip fracture protection was shown (Martens, 2003; Silverman, 2003). Although approved by the FDA for osteoporosis treatment, calcitonin is not approved for osteoporosis prevention (Murphy et al., 2003).

2.8.3.2. Anabolic Agents

The other alternative treatment is bone formation medication such as a PTH hormone (Forteo), which, in contrast to the anti-resorptive agents mentioned above, stimulates new bone formation, restores bone architecture (McClung, 2003) and significantly increases BMD. Forteo received FDA approval in November 2002. It was shown that PTH reduced the risk of new non-vertebral fractures by 35 to 40% in a dose-dependent manner (daily 20 to 40 µg respectively); vertebral fractures were also significantly reduced by 60-70% after 21 months of treatment (Neer et al., 2001). PTH is an attractive alternative for patients who are intolerant of the other anti-resorptive treatments.

2.8.3.3. Combination Treatments

Data comparing bone density increments in men and postmenopausal women showed that PTH hormone acted better than PTH and alendronate combined, which in turn acted better than alendronate alone (Black et al., 2003; Finkelstein et al., 2003). However, other studies have shown that the combination of PTH and estrogen produced greater gains on lumbar and femoral BMD than estrogen alone (Cosman et al., 2001). Other studies have shown that the combination

of estrogen and bisphosphonates together had a greater impact on BMD gains as compared to either agent alone (Bone et al., 2000). Moreover, the combination of calcium, exercise and HRT was evaluated in some studies, where it was shown that estrogen combined with weight-bearing exercises (Kohrt et al., 1995) or resistance exercise (Notelovitz et al., 1991) or even weight bearing plus calcium (Prince et al., 1991) acted better than either treatment alone.

An attractive combination to increase bone strength would be to increase BMD by one of the anti-resorptive agents and to improve bone geometry and architecture by exercise (Uusi-Rasi et al., 2003).

Further studies with fractures as an endpoint need to be implemented before recommending combination therapy to patients with osteoporosis. It is important to note that HRT is no longer viewed as the ‘gold standard’ therapy for osteoporosis (Compston, 2000) owing to the other emerging anti-resorptive and anabolic treatments.

2.8.4. Exercise

Exercise is an important component for a healthy well-being throughout the life cycle; from maximizing peak bone mass during childhood and adolescence, to maintaining or increasing BMD in pre and postmenopausal women, to increasing muscle strength, muscle mass and improving balance in elderly, exercise should be incorporated in everyone’s daily routine. Weight-bearing and resistance training appear to be the first-line exercises that show benefits on BMD in the aging population. Yet, weight-bearing activities (walking) that decrease the risk of trauma may represent a more adequate regimen for elderly males and females who cannot afford lifting weights. Regardless of changes in BMD, the overall benefits of physical activity on the muscles may end up reducing the risk of falling (Lewis and Modlesky, 1998). Toned muscles may also prevent trauma to the bones (Kuntze et al., 1989). Conversely, excessive exercise can

be detrimental in premenopausal women especially in cases of excessive weight loss and secondary amenorrhea (Bubbear and Keen, 2003). According to Wallace and Cumming (2000), optimal training programs to maximize peak bone mass and preserve skeletal integrity are yet to be determined.

2.9. Exercise and Bone Mineral Density (BMD)

According to Turner and Robling (2003), BMD or BMC should not be used as a surrogate measure for bone strength. It should be emphasized that bone strength is a combination of BMD and bone geometry. This being said, albeit the effect of exercise on BMD might be modest, the authors showed in their loading study on rats that it actually resulted in favorable alterations in bone geometry, leading to a great increase in bone strength. Bearing this idea in mind, we reported some of the studies done on postmenopausal women according to the design followed: randomized controlled trials; non-randomized controlled trials; and descriptive studies.

Table 2.1. Randomized Controlled Trials (RCT)

Source	Intervention	Participants	BMD assessment
1-Chan et al., 2004	-Tai Chi Chun (TCC), 45 min/day; 5x/week for 12 months -TCC=low impact weight bearing exercises involving major muscle groups	-Healthy early postmenopausal women (mean age 54 yr) -CG (n=67); -TCC (n=65);	A 2.6 to 3.6 fold retardation bone loss in tibia (cortical + trabecular) in TCC group
2-Verschueren et al., 2004	Whole body vibration (WBV) training; for 6 months	-Postmenopausal women (58-74 yrs) -WBV (n=25); -Resistance(n=22); -CG (n=23)	-BMD of the hip increased (+0.93%, P<0.05) but not total BMD nor lumbar; -Isometric + dynamic muscle strength increased
(Table continued)			

3-Villareal DT et al, 2003	<ul style="list-style-type: none"> -Exercise Group (EG): Physical therapy; resistance; endurance -Home Exercise (HE): Physical therapy; for 9 months -1200 mg Calcium supplements (Ca Supp) + 800 IU vitamin D/day for both groups 	<ul style="list-style-type: none"> -Men and women (≥ 78 yrs) -EG(n=650); -HE (n=47) 	No significant differences in BMD changes between the 2 groups
4-Vincent and Braith, 2002	<ul style="list-style-type: none"> -Progressive Resistance Training (PRE): hi (HI)- or (80% of 1 RM) lo-intensity (LI) -For 6 months; 3x/wk 	<ul style="list-style-type: none"> -Elderly men and women -HI (n=22); -LI (n=24); -CG (n=16); 	<ul style="list-style-type: none"> -BMD for femoral neck increased by 1.96% in HI group. -Total strength increased in HI (17.8%) and LI (17.2%) groups.
5-Kerr et al., 2001	<ul style="list-style-type: none"> -Strength (SG): 3 sets of exercises + progressive increased loading; -Fitness (FG): 3 sets of exercises + bike riding; -Both groups: 3x/wk for 2 years; 600 mg Ca Supp./day 	<ul style="list-style-type: none"> -Postmenopausal women (60 ± 5 years) -FG: n=42 -SG: n=42 -CG: n=42 	<ul style="list-style-type: none"> -A 0.9% increase in BMD the S group at the hip site. -No difference in forearm, lumbar, and whole body BMD between the 2 groups -More retention in the F groups;
6-Maddalozzo and Snow, 2000	<ul style="list-style-type: none"> -High Intensity Resistance Training (HI) -Moderate weight training (MI) -For 6 months, 3x/wk 	<ul style="list-style-type: none"> -Older men and women with no ERT (52-54 years) -HI: n=27 -MI: n=27 	<ul style="list-style-type: none"> -Lumbar BMD increased in HI in men -Hip BMD increased in HI and MI in men -Muscular strength increased in both
7-Rhodes et al., 2000	<ul style="list-style-type: none"> -PRE: 3 sets of 8 reps for large muscle groups; 1 hour session; 3x/wk; for 1 year. 	<ul style="list-style-type: none"> -Healthy sedentary women (mean age 68.8 years) -EG: n=20 -CG: n=18 	<ul style="list-style-type: none"> -No significant changes in BMD between both groups -Increase in muscle strength in EG. -Significant correlations between strength gain (quadriceps) and BMD (lumbar) in EG.
8-Hakkinen et al., 1999	<ul style="list-style-type: none"> -Dynamic Strength Training (DS); 2x/wk; for 12 months + Recreational physical activity (RP) 	<ul style="list-style-type: none"> -Patients with early rheumatoid arthritis -EG: n=32 (DS+RP) -CG: n=33(RP) 	<ul style="list-style-type: none"> -EG increased in muscle strength but not significant changes in BMD -Subjects on glucocorticoids had lower femoral BMD

(Table continued)

9-De Jong et al., 1999	-A 17-week: supplements (S); exercise (E); both (SE); none.	-Frail elderly persons (mean age 78.6 years) -E: n=39 -S: n=41 -SE: n=44 -None: n=37	-S showed increase in BMD, bone mass, and calcium -E showed preservation in muscle mass
10-Kerr et al., 1996	- One year PRE. -Strength (SG)=3x8 RM; -Endurance (En G)=3x20 RM; -1 year	-Early postmenopausal women (mean age 56-58) -En G: n=28 -SG: n=28	-BMD increased site specifically in the SG but not in the En G. -Muscle strength increased in both groups. -Peak load is more important than number of loading cycles
11-Lord et al., 1996	-Structured exercise (warm-up; conditioning; stretching); 1 hour session; 2x/wk; -12 months (four 10-12 weeks session)	-Older women (60-85 years) -EG: n=100 -CG: n=97	-EG: increased strength and sway but not BMD -Overall fracture risk decreased in EG
12-Pruitt et al., 1995	-12 month resistance training program: 10 exercises; 3 days/wk; -High Intensity (HI): 80% of 1-RM -Low-Intensity (LI): 40% of 1-RM	-Healthy older women (65-79 years) -HI: n=8 -LI: n=7 -CG: n=11	-No significant changes in BMD among the 3 groups -Muscular strength increased in the HI and LI.
13-McCartney et al., 1995	-42 weeks of progressive weight-lifting -EG: 2x/wk at 50-80% of 1-RM -CG: usual daily activities	-Males and females (60-80 years) -EG: 37 females + 39 males -CG: 42 females + 24 males	-No change in BMD -Increase in dynamic muscle strength; muscle size; and functional capacity.
14-Nichols et al., 1995	-High-intensity resistance program: 8 exercises; 3 sets; 10-12 reps; at 80% 1RM 3x/wk ⁻¹ for 1 yr	-17 Active elderly women (≥ 60 yrs) -EG: n=9 -CG: n=7	-No significant increases in BMD were found in EG
15-Nelson et al., 1994	-High Intensity strength training (SG); 2x/wk; 5 different exercises; -1 year duration	-Sedentary, no HRT, postmenopausal women (50-70 years) -SG: n=20 -CG: n=20	-Femoral neck and lumbar BMD increased in SG (0.9%; 1% respectively) -Muscle strength; mass; dynamic balance increased in SG

(Table continued)

16- Notelovitz et al., 1991	-Variable-resistance weight training (E) ± estrogen therapy (EST) -Duration of 1 year	-Surgically menopausal women -EST: n=11 -E+EST: n=9	-Lumbar, total, and radial midshaft BMD increased in E+EST (8.3%; 2.1%; 4.1% respectively) and was maintained in EST.
17-Beverly et al., 1989	-Squeezing a tennis ball as hard as possible for 30 seconds each day for 6 weeks.	-99 women (30 had a fractured forearm)	-BMC and strength increased (3.4%; 14.5% respectively) in the stressed forearms -After 6 months of no exercise, only the injured women kept on gaining strength and BMC. All the rest lost previous gains.
18-Sinaki et al., 1989	-Non-loading exercises for back extensor muscles, 1x/day, 5x/week; with a backpack containing sandbag weights -Duration 2 years -No calcium, vitamin D, or estrogen supplementation	-Healthy Caucasian women (49-65 years) with no risk factors for osteoporosis -EG: n=34 -CG: n=31	-Back extensor muscle strength increased in both groups, but more in EG -Mean rate of bone loss was the same in both groups
19- Dalsky et al., 1988	-Weight-bearing exercises; walking; jogging; stair climbing -Duration of 9 months	-Postmenopausal women (55-70 yrs)	-EG increased in BMD (+5.2%); CG decreased in BMD (-1.4%) -No correlation between VO2 max and BMC in EG

Randomized intervention trials are the best studies to show causal inferences (Wolff et al., 1999). Among the 19 studies reported above, 9 of them (3; 7; 8; 9; 11; 12; 13; 14; 18) did not show significant increase in BMD at neither the hip nor the spine area. Ten of them (1; 2; 4; 5; 6; 10; 15; 16; 17; 19) showed a significant increase in BMD in at least one of the skeletal areas (hip or spine).

A myriad of reasons exist to interpret the conflicting results. Some of them are the duration of the study (6 months up to 2 years); the age of the participants (early postmenopausal, late postmenopausal women, or frail); the type of physical activities; the frequency, duration, and intensity of the exercise regimen; the initial BMD of the participants; the estrogen

deficiency; calcium and vitamin D supplementation; the sites and the techniques used to measure BMD; as well as the sample size. Moreover, according to Drinkwater (1994), disparities arise due to the different nomenclature used in specifying the types of the exercise regimen. For instance, “weight bearing or non-weight bearing; loading or non-loading; resistance or endurance”; this makes it hard to determine which kind of exercise is in fact osteogenic. In fact, what is a weight-bearing activity for an individual may or may not be a sufficient loading exercise, owing to the initial BMD and fitness level of the individual. For this purpose, Caldwell J. (1996) has identified these different types of exercises to circumvent this problem:

Table 2.2: Caldwell’s Definitions of Different Exercise Types.

Exercise type	Implication
Passive	Performed by someone else on the subject’s limbs
Active	Performed by the subject him/herself
Isometric active	Contraction of the muscle for a short period with no movement
Isokinetic	Joint motion
Aerobic	At least 15 to 20 minutes of prolonged activity
Anaerobic	Small number of reps with a short time till exhaustion

Based on the RCT studies that showed a significant effect on the BMD, it is suggested that high-intensity exercise (high magnitude with fewer reps) is more efficient in increasing the site specific BMD than the low intensity exercise. This is concordant with the findings of Skerry (1997) who recommended the long-term, progressive high-load with few reps exercises in order to promote osteogenesis. This phenomenon could be explained by the versatile strain distributions that are created throughout the bone. However, according to Karlsson et al., (2001), none of these trials considered fracture rates as an end-point. This might be due to the difficulty in conducting a randomized controlled trial that would last for several years to ascertain fracture incidence.

Congruent with the finding of Villareal et al., (2003), Beck and Snow (2003) reported that to induce increase in bone mass, the impact of the exercise has to cause a bone load that overrides the one resulting from the regular daily activities. Likewise, Westerlind et al. (1997) have shown in a study on ovariectomized (OVX) female rats that mechanical strain (such as treadmill exercise) balances bone formation and bone resorption in OVX rat, while bone loss occurs in OVX rats in sites with low strain. Nevertheless, for individuals with osteoporosis, strenuous high impact activities may be detrimental to their skeletal health. Examples of such activities to be avoided include jumping, running, or even trunk flexion activities such as toe touches, rowing, and full sit-ups (Meeks, 1999).

Drinkwater (1994) has provided a logical interpretation of the literature based on the five basic principles of the physical training, which are: (1) Specificity, which implies that an exercise should be designed to target a specific target bone; (2) Overload, which means that an exercise should cause an overload on the bone which exceeds a certain remodeling threshold in order to stimulate osteogenesis; (3) Reversibility, which means that if the exercise is stopped, the increase in BMD is reversed or lost; (4) Initial values, which suggests that the baseline BMD or fitness level does affect the subsequent results of the exercise on the BMD, where people with a lower baseline value are more prone to see improvement than those who have a higher baseline values; and (5) diminishing returns, which suggests that early responses of the bone are more marked than the subsequent responses, may be because the subject would be approaching his/her “biological ceiling.”

A recent meta-analysis of randomized trials between 1977 and 1996 was conducted by Wallace and Cumming in 2000. They classified the exercises under 2 categories: “Impact” (walking, running, aerobics, and heel drops) and “non-impact” which reflects to all kind of

strength training with weights (free weights, weight machines, or weighted backpacks) also known as resistance training, weight lifting, and strength training. Yet, they did not examine the impact of exercise frequency or duration in their meta-analysis. The meta-analysis found that the impact exercises yielded a significant increase in lumbar BMD (1.5%) and femoral neck BMD (1%) in both pre- and postmenopausal women. As for the non-impact exercises, they had a positive effect on the lumbar spine (1%) regardless of the menopausal status, but conclusions could not be drawn on their effect on the femoral neck BMD owing to the paucity of the studies.

Although some researchers concluded from their study in rats that increasing load frequency was more important than increasing load intensity in order to promote osteogenesis (Hsieh and Turner, 2001; Turner and Robling, 2003), other authors have showed the opposite. Vincent and Braith (2002) (study 4) concluded that 1 set of high resistance training was effective in increasing BMD in elderly men and women; likewise, Kerr et al (1996) (study 10) showed that the peak load with low reps was a more important factor in achieving bone gain than the low load endurance exercise. Similarly, Martin and McCulloch (1987) stressed more importance on the intensity rather than the frequency of the stimulus. Congruently, Snow-Harter et al., (1992) found significant increases with a similar program in postmenopausal women. Strikingly, two other studies have found no significant increases on BMD upon high resistance exercise (Nichols et al., 1995; Pruitt et al., 1992). In both of these studies, however, selected subjects were healthy and had a good baseline BMD.

Table 2.3. Non Randomized Controlled Trials (NRCT)

Source	Intervention	Participants	BMD assessment
1-Yamazaki et al., 2004	-Moderate walking exercise; at 50% VO2 max; for at least 1 hour; 4x/week; -Duration of 1 year	- Postmenopausal women with osteopenia/osteoporosis -EG (n=32); -CG (n=18);	-Lumbar BMD increased in the EG and did not change in CG
(Table continued)			

2-Kemmler et al., 2004	<ul style="list-style-type: none"> -Intense exercise: 2 group sessions and 2 home sessions per week -Calcium supplements and cholecalciferol to all -Duration of 2 years 	<ul style="list-style-type: none"> -Early postmenopausal osteopenic women -EG (n=50); -CG (n=33); 	<ul style="list-style-type: none"> -Lumbar BMD increased in EG (0.7%) -Decrease in rate of hip bone loss in the EG (-0.3%) vs. CG (-1.7%)
3-Wu et al., 2000	<ul style="list-style-type: none"> -Swimming; 1 hour; 1.5 sessions per week; -Duration of 2 years 	<ul style="list-style-type: none"> -Post menopausal women -EG: n=22 (mean age 59.5) -CG: n=19 (mean age 59.3) 	<ul style="list-style-type: none"> -EG had higher BMD in hip region but had decreased BMD in spine -Muscle leg strength increased in EG
4-Humphries et al., 2000	<ul style="list-style-type: none"> -Short term high intensity strength training (weights):60-90% 1RM; or 50-min low intensity walking ± HRT; 2x/wk -Duration of 24 weeks 	<ul style="list-style-type: none"> -Older women (45-65 yrs) -Weights: n=21 -Walking: n=20 -Weights+ HRT: n=14 -Walking+ HRT: n=9 	<ul style="list-style-type: none"> -No difference in lumbar BMD among groups. -Muscular strength increased in Weights and Weights+ HRT groups
5-Pruitt et al., 1992	<ul style="list-style-type: none"> -Weight training; 1 hour session (warm-up-weights-stretching); 3x/wk; duration of 9 months 	<ul style="list-style-type: none"> -Early postmenopausal women -EG: n=17 -CG: n=9 	<ul style="list-style-type: none"> -Lumbar BMD increased in EG (+1.6%) -No changes in hip or distal wrist BMD in EG
6-Sinaki et al., 1984	<ul style="list-style-type: none"> -Flexion (F) vs. Extension (E) exercises or None (N) -Follow-up from 1 to 6 years 	<ul style="list-style-type: none"> -Postmenopausal women (49-60 yrs) -F: n=9 -E: n=25 -F+E: n=19 -N: n=6 	<ul style="list-style-type: none"> -Compression fractures occurred mostly in F: 89%; N: 67%; E+F: 53%; E: 16%. -Flexion exercises are not appropriate.

As for the non-randomized controlled trials, study 4 did not show a significant change in BMD, studies 3 and 5 showed some site-specific effects on BMD, and the rest of the studies did show a significant increase in BMD. Again, these conflicting results go back to the same reasons mentioned above. In fact, according to Wolff et al., (1999), non-randomized controlled trials tend to positively bias the results by magnifying the effects to more than what they should be, owing to the non-randomization confounding bias.

In a recent meta-analysis of randomized and non-randomized controlled trials between 1966 and 1996 conducted by Wolff and his coworkers in 1999, they concluded that the exercise training program did in fact suppress or reverse bone loss rate by almost 1% per year, irrespective to the menopausal status. Yet, specific exercise recommendations could not be developed owing to the variety of the exercise type, duration, intensity, and frequency used in these studies.

Table 2.4. Descriptive Studies

Source	Design	Participants	Comments
1-Sran and Khan, 2005	-Survey about physiotherapy and osteoporosis; -Cross sectional study	-171 physiotherapists; -Response rate 39 %;	-45% used manual therapy -91% had concerns such as vertebral and rib fractures owing to manual therapy in osteoporotic patients
2-Kemmler et al., 2004	-Cross-sectional	-150 early postmenopausal osteopenic women (PMW) (mean age 55.5)	-Weak relationship between habitual physical activity/non athletic exercise on bone parameters in early PMW
3-Devine et al., 2004	-Cross-sectional	-1363 older women (mean age 75)	-Hip BMD was higher by 5.1% in those who achieved physical activity (4 hrs of walking or more/wk) and dietary calcium intake (>800mg/day)
4-Greendale et al., 2003	-Cross sectional -Adjusted linear regression	N =544 African American N =1044 Caucasian N =230 Chinese N =239 Japanese	-Higher sport and home physical activity (PA) were associated with higher lumbar and hip BMD. -Work PA or active living were not associated to BMD
5-Owings et al., 2002	-Cross sectional (Correlational)	50 older women and 29 older men; healthy; not doing resistance training	-Correlation between hip BMD and muscle strength of the lower joints depends on body size in healthy older adults
6-Sinaki et al., 1996	-Cross sectional	-36 women with osteoporosis (47-84 years)	-There was a negative correlation between: -Back extensor strength and the number of vertebral compression fractures (VCF) - BMD and number of VCF

(Table Continued)

7-Heinonen et al., 1993	-Cross-sectional -ANOVA	30 female orienteers; 28 cross-country skiers; 29 cyclists; 18 weight lifters; 25 reference group	-BMD was higher in weight lifters than in referents -Of the endurance athletes, only orienteers had higher BMD than referents
8-Michel et al., 1989	-Cross-sectional	78 healthy subjects (>50 years)	-Weight-bearing exercise (up to 300 min/wk) was strongly correlated with lumbar BMD in women -Extremely vigorous exercise may be detrimental to individuals>50 years
9-Pocock et al., 1986	-Cross-sectional	46 postmenopausal subjects among 84 Caucasian (age 20-75 yrs)	-Fitness predicted femoral neck BMD and fitness and weight predicted lumbar BMD in the 46 postmenopausal women
10-Stillman et al., 1986	-Cross-sectional -Activity categorized (1-5) or very sedentary to very active	-Women aged 30-85 yrs: High active groups: n=28 Moderate active: n=36; Low active: n=19	-BMC was higher in high active groups than the low active group; No difference between moderate and low active groups.

Descriptive studies can never show causality. They only show correlations and they also generate hypotheses that need to be tested by controlled trials. They are also subject to selection bias (Wolff et al., 1999). In general, most of these studies summarized in the table above (3; 4; 7; 8; 9; 10) reflect a relationship between weight-bearing physical activity and resistance training with BMC or BMD. The notion of site-specificity is also remarkable where the BMD increases only in the specific bones attached to the muscles engaged in the physical activity. The drawback of descriptive studies is that we can never prove which factor lead to the other. For instance, did BMD increase because of physical activity or did a healthy skeletal bone lead to a physically active lifestyle? These questions can be answered by the controlled clinical trials.

2.10. Exercise and Muscle Strength

Clark (1996) gave details in his book about strength training for the aging adult. He defined muscle strength as “the ability of the muscle to perform some tasks of daily living such

as lifting, carrying, pushing, pulling, sitting, standing, walking, and climbing stairs”. According to Clark, exercise can influence some fitness parameters such as muscle strength, range of motion, and balance. Luckily, muscle strength does not decline exponentially as bone does owing to the lack of estrogen after menopause (Sinaki, 2003). The loss of muscle strength occurs gradually with aging as muscle mass declines (Rogers and Evans, 1993) and as the result of lack of physical activity. Thus, skeletal deformity occurs and the incidence of falls accrues (Sinaki, 2003). When the strength of the trunk is lost, specifically the back extensor strength, vertebral fractures may result (Hertel and Trahiotis, 2001). The studies related to exercise and muscle strength in postmenopausal women were reported according to the design followed:

Table 2.5. Randomized Controlled Trials (RCT)

Source	Intervention	Participants	Strength assessment
1-Gold et al., 2004	-Modified cross-over -EG: 6 months exercise (phase 1) + 6 months self-maintenance (phase 2) -CG: 6 months self maintenance (phase 1) + 6 months exercise (phase 2)	-185 postmenopausal Caucasian women (mean age 81), each with at least 1 vertebral fracture (VF) -EG: n=94 -CG: n=91	-In phase 1, EG had higher extension strength than CG; -In phase 2, CG had significant changes in trunk strength from baseline. EG did not maintain their improved trunk strength.
2-Kemmler et al., 2004	-Modified cross-over -G1: 12 wks high intensity (HI) multiple set + 5 wks low intensity training + 12 weeks HI single set; -G2: 12 wks HI single set + 5 wks low intensity + 12 weeks HI multiple set;	-Well trained early post-menopausal women (1-8 yrs after menopause) -G1: n=29; -G2: n=21	-Multiple set HI trainings resulted in higher strength increases (3.3-5.5%) -Single set HI training resulted in significant decreases (-1.1 to -2%) -Multiple set protocols HI increase muscle strength more than single set HI protocols
3-Vincent et al., 2002	-high intensity (HI): 80% of 1 RM; 8 reps; -low intensity (LI): 50% of 1 RM; 13 reps; -1 set of 12 exercises. -Duration for 6 months	-Adults aged 60 to 83 yrs -HI: n=22 -LI: n=24 -CG: n=16	-Significant improvements in strength, endurance, and stair climbing time in both groups. -HI or LI have similar strength benefits in elderly

(Table Continued)

4-Carter et al., 2002	-Community based exercise program -Twice weekly exercise class for 20 wks	-65 to 75 yr old women with osteoporosis -EG: n=40 -CG: n=40	-Improvement in dynamic balance (3.3%) and strength (7.8%) in the EG, i.e. reduced risk factor for falls
5-Bemben et al., 2000	-High intensity (HI) (80% 1 RM; 8 reps) -Low intensity (LI) (40% 1 RM; 16 reps) -Duration: 6 months; Volume: 3 sets, 3d.wk ⁻¹ -12 exercises that load spine and hip -Ca supp to 1500mg.d ⁻¹	-Early estrogen deficient postmenopausal women (41-60 yrs) -HI: n=10 -LI: n=7 -CG: n=8	-HI and LI had similar increases in muscle strength (biceps; lower body; hip; rectus femoris). -HI had higher upper body strength than LI. -Neither group had increase in hip or spine BMD
6-Itoi and Sinaki, 1994	-back-strengthening exercises -Duration of 2 yrs	-Healthy estrogen deficient women (49-65 yrs) -EG: n=32 -CG: n=28	-Back extensor strength increased significantly in both groups. -EG had less thoracic kyphosis.
7-Morgan et al., 1995	-Aerobics exercise (A) ± strength training (S) (3 sets of 8-12 reps of knee exercises; 80% 1RM); Duration: A=8 months; S=3x/wk; 3 wks	-Aerobically active post-menopausal women (61-71yrs) -A+S: n=9 -A: n=9	-A+S group had highly significant increases in knee flexion and extension strength. -Resistance is a crucial supplement to aerobics to increase muscle strength.
8-Morganti et al., 1995	-Progressive Resistance training (PRT) at ≥ 80% of 1 RM; 2x/wk; -Duration of 1 yr	-Older healthy women (mean age 59.5) -PRT: n=21 -CG: n=19	-In all exercises, PRT had substantial, continual strength gains, with the greatest gains in the first 3 months of training
9-Charette et al., 1991	-12 wk Resistance training: 7 exercises for the lower extremities	-Older women (mean age 69 yr) -EG: n=13 -CG: n=6	-EG had significant increases in muscle strength (28-115%) and in cross-sectional area of type II muscle fibers (20.1%) as compared to baseline values

Most of the above mentioned RCT (3; 5) suggested that high intensity (HI) or low intensity (LI) strength exercises had similar effects on increasing muscle strength; study 2 showed that HI single set strength training resulted in a decrease in strength as compared to HI multiple set strength training, contrary to what study 3 has showed, where one set of HI did

actually improve muscle strength. These inconsistencies may stem from the difference in the baseline values of the individuals, where in study 2 they were well trained and in study 3 they were not. Similarly, study 5 showed that HI and LI strength training had similar increases on muscle strength, and again, the authors used a different number of sets in the exercises. The same five basic principles of the physical training explained above apply in the discussion of the discrepancies of the results. Yet, this empirical evidence converges to the same conclusion, which is that the resistance training with different intensities can significantly improve muscle strength, and thus reduce the risk of falls. According to Sinaki (2003), proper rehabilitation programs can significantly reduce the musculoskeletal deformities owing to osteoporosis. This non-pharmacologic intervention is based on empirical evidence resulting from controlled trials.

Table 2.6. Non Randomized Controlled Trials (NRCT)

Source	Intervention	Participants	BMD assessment
1-Belanger et al., 2000	-Functional electrical stimulation (FES) ± Resistance training (RT) -1 hour a day; 5 days/wk for 24 weeks	- Spinal Cord injured individuals with osteopenia (mean age 33 yrs) -SCI with FES±RT: n=14 (left-resisted vs. right-unresisted quadriceps) -CG (no SCI; no FES): n=14	-SCI with the FES treatment showed increased BMD (in muscle with or without RT) and strength (in resisted muscle) in femur and tibia as compared to the CG.
2-Kerschman-Schindl et al., 2000	-Home exercise program (HEP): calisthenics; 3x/wk for 30 min; against gravity or with bands or gymnastic balls for 9.7 to 10 yrs	-33 postmenopausal women (45-75 yr) with a history of at least 1 fracture and BMD ≤-1SD below the age adjusted mean -EG: n=19 -CG: n=6	-No significant differences in fracture rate, falling episodes, and BMD were observed. -HEP not efficient for this population.

These 2 NRCT suggest that electrical stimulation might be beneficial to treat or reverse osteoporosis by increasing BMD with or without applying resistance. However, muscle strength was only increased when resistance training was performed and not under electrical stimulation. The other study (2) suggested that HEP are not enough to decrease fracture rate in

postmenopausal women; therefore, a more involved exercise regimen needs to be performed by these women to counteract the effects of osteoporosis.

Table 2.7. Descriptive Studies

Source	Design	Participants	Comments
1-Sinaki et al., 1993	-Cross sectional	-Cases: n=55 osteoporotic women (40-85 yrs) -Controls: n=25 healthy women (40-85 yrs)	-After adjusting for age, osteoporotic women had significantly lower back extensor strength (BES) than the normal women; this might lead to skeletal deformities and osteoporosis postural abnormalities
2-Sinaki and McPhee, 1986	-Cross-sectional	-Healthy Caucasian postmenopausal women (n=68)	-A significant positive correlation between lumbar BMD and BES, even after adjusting for age -Positive correlation between BMD and body weight. -High BES may benefit lumbar BMD

These 2 studies suggested a negative correlation between skeletal deformities and BES (study 1) and a positive correlation between a high BES and lumbar BMD (study 2). Yet, due to the type of the descriptive studies, one cannot confirm which one happens first; is it the weakening of the muscles or the skeletal deformities? Or is it the strength of the muscles or the healthy skeletal? Although these studies do not provide confirming answers, strength training does not seem unfavorable for individuals with osteoporosis (Hertel and Trahiotis, 2001).

2.11. Exercise Guidelines

Every physical exercise should include 3 parts: aerobics (walking, cycling, and running), strength, and flexibility. Ideally, the strength component should target all the muscle groups necessary for our daily functional activities (upper body strength, lower body strength, and core/lower back strength). The American College of Sports Medicine (ACSM, 1998) has established some guidelines for the healthy adult suggesting that this latter should perform a

minimum of 8 to 10 exercises for the major muscle groups with a volume of 1 set of 8-12 reps or near fatigue for 2-3 days a week. As for the elderly, Pollock et al. (1994) gave some resistance training guidelines for elderly. He suggested that elderly should perform 8 to 10 exercises for the major muscle groups (chest, back, biceps, triceps, shoulders, hips, legs, and abdominals) with a volume of 1 set of 10 to 15 reps with a frequency of 2 days a week. Nevertheless, no one has yet examined the effect of these exercises on the BMD in elderly men and women (Vincent and Braith, 2002).

Table 2.8. Exercise Guidelines

Source	Group	# of sets	# of reps	# of exercises	# d.wk⁻¹
Pollock et al., 1994	Elderly	1	10-15	8-10	2
ACSM, 1998	Adult	Minimum 1	8-12 or near fatigue	Minimum 8-10	2-3
Rhea et al., 2003	Untrained	4 sets/muscle group	60% 1 RM	All muscle groups	3 (each muscle group)
Rhea et al., 2003	Trained	4 sets/muscle group	80% 1 RM	All muscle groups	2 (each muscle group)

As a follow-up to the previous statement, the ACSM conducted a subsequent statement saying that as the training proceeds, the volume (number of sets) and the intensity (% of 1 RM) of the workout have to gradually increase in order to stimulate the neuromuscular system. The amount of increase in strength was not given with specific volume and intensity. As a corollary, Rhea et al. (2003) came up with a formula out of a meta-analysis of 140 studies. This formula calculated the effect size (ES) to quantify the dose-response relationship for strength accrual. Accordingly, they came up with the guidelines for trained and untrained individuals. Thus, to elicit maximum strength gain in trained individuals, they should perform 4 sets for each muscle groups at 80% 1RM 2 days a week. Whereas untrained individuals should perform 4 sets for each muscle groups at 60% 1RM 3 days a week. Further studies need to be implemented to test

whether these recommendations of dose-response relationship for muscular strength development can be applied in patients with osteopenia/osteoporosis.

2.12. Summary

To sum up, osteoporosis is a skeletal disorder that predisposes the person to an increased risk of fracture. The trabecular bone is more susceptible to osteoporosis than the cortical bone. Fractures occurring as a result of osteoporosis can be life threatening to the patient. Management of this disease depends on its prevention, diagnosis, and treatment. Prevention starts at an early age by having an appropriate calcium intake and adopting an active lifestyle; it continues through adulthood by avoiding excessive alcohol, caffeine, and cigarette smoking among other factors. Diagnosis identifies the risk factors of osteoporosis and prompts a DXA scan if the disease is suspected. Treatment of osteoporosis includes pharmacological and non-pharmacological agents. The former (pharmacological) includes anti-resorptive therapy such as hormones, bisphosphonates, SERM, calcitonin, as well as anabolic agents such as the PTH Forteo. The latter (non-pharmacological) includes calcium intake and exercise.

Results have been inconsistent with respect to the protective effect of exercise on bone loss at the spine and hip. This is partly due to the difference in the study design (RCT, NRCT, and descriptive studies) as well as the complex interaction of the bone with different factors (diet, age, genetics, hormones). However, all of the studies have been consistent with respect to the weight bearing exercise and resistance training imparting an increase in muscle strength. Consequently, exercise should be included in everyone's lifestyle in order to maximize peak bone mass, maintain muscle balance and strength, optimize bone geometry and strength (Beck and Snow, 2003), reduce or suppress bone loss, and thus minimize the propensity to fall. Albeit the strength training effect on BMD might be modest, exercise still plays an important role in

decreasing the incidence of fractures by optimizing the skeletal health. Therefore, an optimal exercise prescription for elderly should target exercises that focus on increasing muscle strength, balance, and agility, as well as the bones involved in weight bearing activities, yet, without causing a high stress threatening their bones. In fact, The American Geriatrics Society (AGS, 2001) recommends in a published guide that elderly people engage in physical activities that optimize their balance and they should avoid the potential hazards that would cause them to fall in the home (loose carpets, misplaced items, dim lighting).

2.13. Future Studies' Suggestions

Future research should focus on conducting long-term, large randomized controlled trials to study the effect of novel exercise modalities, with conjunction of calcium and vitamin D supplementation, on fracture risk reduction in patients with osteoporosis. Further research must test the dose-response relationship in muscle strength gain in trained and untrained people and check if this principle applies in elderly with osteopenia/osteoporosis. Moreover, there is a definite need to adopt a standardized nomenclature to the different exercises used and the different sites measured, bearing in mind the concept of the baseline BMD values as well as the concept of the regression to the mean for participants with extreme scores. Ultimately, exercise recommendations for elderly subjects with osteoporosis should focus more on reducing the risk of falls and lowering the exercise intensities.

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CHAPTER III

SURVEY OF BATON ROUGE/NEW ORLEANS PHYSICIANS WHO MANAGE OSTEOPOROSIS

3.1. Introduction

According to the National Institute of Health (NIH), “osteoporosis is defined as a skeletal disorder characterized by compromised bone strength” predisposing a person to an elevated fracture risk. Bone strength primarily reflects the integration of bone density (grams of calcium per unit area or volume of bone) and bone quality (micro architecture of bone) (NIH, 2001). The World Health Organization (WHO) operationally defines osteoporosis as “bone density 2.5 S.Ds below the mean for the young white adult women”.

It has been estimated that osteoporosis affects approximately 25 million people in the United States and mostly women (McCoy, 2001). If untreated, “osteoporosis can be one of the leading causes of suffering, disability, and death in elderly people” (Goldmann and Horowitz, 2000). Osteoporotic fractures represent a major and escalating “threat to our aging population” (Melton, 2000).

Osteoporosis is both “preventable and treatable” (Eastell, 1998), yet, according to McCoy (2001) it is often “undiagnosed and untreated”. Cuddihy et al. (2002) have shown that “effective osteoporosis interventions are underutilized among postmenopausal women” who experience a fracture due to osteoporosis. The WHO and the National Osteoporosis Foundation (NOF) of the United States have both established guidelines for the physicians to prevent, diagnose, and treat osteoporosis. However, there are some discrepancies between both guidelines, and according to some studies (Wilkin and Eastell, 1999; Hui et al., 1988) osteoporosis diagnosis has been controversial. Nevertheless, osteoporosis diagnosis depends to a greater extent on the knowledge of the physicians (Werner and Vered, 2002).

3.1.1. Purpose

The purpose of the survey was to collect descriptive information on how physicians who treat osteoporosis in Baton Rouge/New Orleans communities diagnose, prevent, treat, and follow up with osteoporosis patients, and how the physicians' recommendations compare with standards (WHO; NOF) according to their area of specialty and their years of experience.

3.2. Materials and Methods

Four hundred questionnaires (Appendix 1) were distributed to a stratified sample of physicians. The sample was selected according to physician's specialty and geographic location. The specialties that were targeted were rheumatology (Rheum), family medicine (FP), orthopedics (Ortho), internal medicine (IM), obstetrics and gynecology (ObGyn), endocrinology (Endo), and others. The questionnaires were first drafted, pre-tested, and modified after a pilot survey on a small sample of physicians. The questionnaires were then delivered to different locations in Baton Rouge and New Orleans, along with a cover letter and a self-addressed stamped envelope. Once completed, the questionnaires were mailed back, faxed to LSU school of Human Ecology, or picked up from their location by the investigator. For analysis purposes, physician's specialty was divided into 5 broad categories: internal medicine, obstetrics and gynecologists, family practitioner + nurse practitioners, orthopedics + others, and endocrinologists + rheumatologist. Physicians' years of experience ranged between 1 year and ≥ 25 years. Overall, 106 questionnaires were returned back, and five were removed because the physicians didn't treat osteoporosis, therefore, the overall response rate was 25%.

The structured questionnaire was comprised of the following information:

1. Physicians' demographic information and professional background: area of specialty, years of experience, place of work, number of patients seen per month.

2. Knowledge about osteoporosis prevention: One multiple choice closed-ended question was used.
3. Knowledge about osteoporosis diagnosis: four multiple choice closed ended questions were used.
4. Knowledge about osteoporosis treatment: two multiple choice questions were used, of which one had 6 subheadings.
5. Knowledge about osteoporosis follow-up: two multiple choice questions were used. Another two questions regarding follow-up were dropped out of the analysis because of the missing values.
6. Patients' demographic information: age range, distribution of sex and race, areas mostly affected.

Correct answers to the knowledge items were based on the guidelines published by WHO and NOF, as well as other published references, and are summarized in appendix 2

3.2.1. Data Analysis and Statistical Methods

Data were analyzed in several steps. First, descriptive statistics, which include percentages of correct answers and proportions of variables, were computed. Second, comparative statistics, which includes hypothesis testing about osteoporosis management; Osteoporosis management included the three questions corresponding to prevention, diagnosis, and treatment of osteoporosis. Each question consisted of a set of multiple choice answers where the physicians had to mark the correct answers. The participants received a score of “1” for a correct answer and a score of “0” for an incorrect answer. A total score was calculated across the different questions to determine knowledge about osteoporosis management on a 3 subscales: prevention, diagnosis, and treatment. A cut-off point was chosen where if 80% of the answers

were marked right, then the corresponding question would be marked as correct. Thus, each of the three responses was treated as a binary outcome. The two independent variables were area of specialty and years of experience. Area of specialty was treated as a categorical variable and years of experience was kept as a continuous variable. The three binary responses were treated as a repeated measure on each subject. Repeated measures analysis with discrete data using the SAS system (Proc Genmod) was used to test whether the knowledge among physicians varied according to their area of specialty and their years of experience. Conditional odds ratio (OR) with associated 95% confidence intervals (95%CI) were used to test the significance of the associations among the variables. Analysis of deviance was used to choose the model with the best fit.

3.3. Results

3.3.1. Descriptive Analysis

Table 3.1 indicates that 35% of the respondents' specialty was Internal Medicine and 95 were endocrinologists and rheumatologists.

Table 3.1: Characteristics of the responding physicians according to area of specialty

Specialty	Percentage
Internal Medicine	35
Obstetrics and Gynecologists	25
Family Practitioner + Nurse Practitioner	16
Orthopedics and Others*	15
Endocrinologist + Rheumatologist	9

*Others include nephrologists, oncologists, and pain management specialists.

Mostly Caucasian females suffer from osteoporosis. In this study, osteoporosis started as early as 28 years of age and as late as 89 years of age. The area that is mostly affected is the spine (62%), followed by the hip (35%). It will be shown in chapter IV that people suffer from low bone mineral density mostly in the spine area.

Table 3.2: Patients' information

Gender		Age	
Mean % females	80% \pm 18.1	Mean maximum age	89 \pm 10.4
Mean % males	20% \pm 18.1	Mean minimum age	28 \pm 17.6
Race		Areas mostly affected	
Caucasian	54.2% \pm 25	Spine	62% \pm 23.9
African American	39.2% \pm 24.4	Hip	35% \pm 22.9
Hispanic	5.63% \pm 10.5	Wrist	5% \pm 12.0
Native American	1.97% \pm 10.1	Other (femur, feet, ribs)	0.84% \pm 4.9

Table 3.3: Percentage of physicians recommending specific strategies for osteoporosis prevention

Preventive measures prescribed before osteoporosis occurs	%Physicians	Correct responses†
High calcium diet and exercise*	98%	Yes
Control of alcohol and smoking*	75%	Yes
Gonadal steroids in men and women if hypogonadal‡§	45%	Yes
Control of caffeine intake	40%	Yes
Control of salt intake	21%	Yes
Others (calcium supplements, exercise, screening, bisphosphonates, PTH assessment)	19%	----
Control of protein intake	12%	Yes

*Recommended by WHO; ‡ Recommended by WHO in women with ovarian failure;

§ Recommended by published reference (Snyder et al., 1999); †correct responses are provided in boldface type

The majority of physicians reported high calcium diet and exercise, as well as control of alcohol and smoking as preventive measures for osteoporosis. Only 45% reported the usage of gonadal steroids in both hypogonadal men and women.

Fracture, loss of height, curved back, family history, smoking, low body weight, and frailty were among the most reported signs of osteoporosis presence by the respondents.

The majority of the respondents reported the usage of DXA scans as a detection before fractures occur. Others also reported history taking and physical examination for osteoporosis diagnosis. Surprisingly, 41% of the respondents reported the usage of X-ray.

Tables 3.4 (a; b; c): Percentage of physicians recommending specific strategies for osteoporosis diagnosis

Table 3.4a:

Signs of osteoporosis presence	% physicians	Correct responses
Fracture*	90	Yes
Loss of height*	88	Yes
Curved back*	84	Yes
Family history*	83	Yes
Smoking*	80	Yes
Low Body Weight*	75	Yes
Frailty	71	Yes
Low Peak Bone Mass (PBM) at early ages	53	Yes
Pain	52	Yes
Other (steroid use, white race, post-menopausal, amenorrhea)*	34	----

***Recommended by WHO**

Table 3.4b:

Detection methods before fractures occur	% physicians	Correct responses
DXA*	90	Yes
History taking	61	Yes
Physical examination	44	Yes
X-ray†	41	No
Blood and urine tests for bone markers	7	Yes
Quantitative ultrasound for bone density	6	Yes
None	2	No

*** Recommended by WHO (Delmas and Fraser, 1999); † X-rays will only detect bone loss by the time 25 ± 40% of bone mass has already gone (Delmas and Fraser, 1999)**

Physicians demonstrated poor knowledge with respect to DXA scan usage upon glucocorticoid usage and for all women above 65 years of age.

Most of the physicians recommended non-pharmacological treatments for osteoporosis such as exercise, dietary changes, and calcium supplements, as well as pharmacological treatments such as bisphosphonates, hormone therapy, and nasal calcitonin.

Walking and resistance training were the priority choices among the majority of the respondents for the kind of exercise for osteoporosis treatment.

Table 3.4c:

Bone density scan recommendation	% physicians	Correct responses
When osteoporosis is suspected, before fractures occur‡	82	Yes
When see clinical risk factors (premature menopause...) ‡	71	Yes
To assess effectiveness of a given treatment‡§	60	Yes
When fractures have already occurred‡	54	Yes
Upon gluco-corticoid use*‡	43	Yes
All postmenopausal women†	39	No
All women above 65 years of age*‡	29	Yes
All post-menopausal women not on hormones†	27	No
Others (women at menopause) †	7	No
All men above 65 years of age†	2	No

*Recommended by NOF; ‡Recommended by WHO; † Not recommended by WHO unless presence of other risk factors; § Recommended by published references (Miller et al., 1999; Bonnick SL, 2000)

Tables 3.5(a- -c): Percentage of physicians recommending specific strategies for osteoporosis treatment:

Table 3.5a:

Treatment	% physicians	Correct responses
Supplements*	100 (Ca 100% ; vitamin D 89%)	Yes
Exercise*	95	Yes
Bisphosphonates‡	92 (Fosamax 90%; Actonel 42%; Etidronate 15%)	Yes
Hormone therapy†	87	Controversial
Diet change*	82 (more dairy 61% and fortified milk 51%)	Yes
Nasal calcitonin‡	47	Yes

*Recommended by WHO; ‡ Recommended by WHO; shown to decrease rate of bone loss in postmenopausal women; † Not recommended by the FDA

Most of the respondents reported estrogen and evista as the types of hormones they would use for osteoporosis treatment.

Fifty percent of the physicians reported that patients came back for a follow-up every 2 years, while 28% reported that patients came back every one year.

Eighty eight percent of the physicians thought that the patients did not follow their prescription (partially 87% or fully 1%), and only 4% thought that the patients followed completely their prescription. ‘Other’ includes answers such as “it depends on the patient”.

Table 3.5b:

Exercise kind	% physicians	Correct responses
Walking*	85	Yes
Resistance*	51	Yes
Swimming**	33	Controversial
Running‡	20	Yes
Non weight bearing‡‡‡	19	No
Physical therapy	16	Controversial
Other (bicycle, weight-bearing)	12	----

*Recommended by NOF; ** The effect of swimming on human bone skeleton is still controversial; ‡Not advised according to Shephard, 2002; ‡‡‡Non weight bearing (bicycling) is not recommended by NOF

Table 3.5c:

Types of hormones*	% physicians
Estrogen	68
Evista	50
Combination of Estrogen & Progesterone	46
Progesterone	19
Testosterone	15
Other	6

*87% of the physicians prescribed HRT as a treatment of osteoporosis

Table 3.6: Frequency of patients coming back for follow-up based on physicians' estimation

Frequency of patients coming back for follow-up	% based on physicians' estimation
Every 2 years	50
Every 1 year	28
Other (never, 3-4 years, no access for DXA)	15
Every 6 months	7

Table 3.7: Physicians' opinion about whether patients follow their prescription

Physician's answer	% physicians
Partially	87%
Missing	6%
Completely	4%
Other	2%
No	1%

3.3.2. Comparative Analysis

Generalized Estimating Equations (GEEs) methodology (Gordon Johnston, SAS Institute, <http://www.ats.ucla.edu/stat/sas/library/gee.pdf>) was used to test whether the knowledge among physicians varied according to their area of specialty (S) and their years of experience (E). Our survey has a moderate number of repeated measures on many subjects. These repeated measures are treated as binary discrete responses (T), which makes the data look like a cross-sectional time series (Liang and Zeger, 1986). When the responses are discrete and correlated, the method of GEEs provides a practical way with reasonable statistical efficiency to analyze such data. The “exchangeable” correlation matrix with Proc Genmod in SAS, along with the “repeated” statement, will account for of the correlation among the responses. As a result, the “population averaged coefficient” or the beta parameters will be estimated. Based on the analysis of deviance (ΔG^2) of the nested models shown in Table 3.8, model (4) was the most appropriate model, where each of the main effects showed significance without any significant interaction among them (Table 9).

Model (4): $\ln \frac{\Pi}{1-\Pi} = \alpha + \beta_i^T + \beta_j^S + \gamma E$

Π = probability of having a correct answer.

$1 - \Pi$ = probability of not answering correctly.

α = intercept

β_i^T = slope for the categorical variable T (time), representing the 3 binary responses.

β_j^S = slope for the categorical variable S (specialty)

γ = slope for the continuous variable E (experience)

The analysis of deviance compares the deviances between two models (one is full and the other is reduced) by taking their difference. Model (1) is the fullest model and has the 2 two-way interactions (E*S) and (E*T) as well as the main effects (E, S and T). Model (2) has one two-way interaction (E*S) and the main effects. The null hypothesis suggests that these two

models have the same goodness of fit. If the resulting P value of this test is greater than 0.05, this means there is failure of rejection of the null hypothesis, which means that the two models have the same goodness of fit and thus we choose the simpler model (2). This analysis is reiterated several times until we come up with the simplest model that is not significantly different from the full model. In our case, model (4) was the chosen model (P=0.1), because it is not significantly different from its previous more complex model (3)

Table 3.8: Analysis of deviance to come up with the best fit model

Model	Predictors	Deviance G^2	df	Models Compared	ΔG^2	Δdf	P value
(1)	E*S; E*T E; S; T	288.07	268	-----	-----	---	---
(2)	E*S E; S; T	292	270	(2)-(1)	3.93	2	0.2
(3)	E*T E; S; T	296.03	272	(3)-(2)	4.03	2	0.1
(4)	E; S; T	300.6	274	(4)-(3)	4.57	2	0.1

E= Years of Experience; S= Area of Specialty; T=Time, which corresponds to the three different questions; prevention, diagnosis, and treatment.

The test of the significance of each effect in model (4) appeared to be significant as shown from the score test in table 3.9. This suggests that there is difference in the correct responses obtained based on the type of question asked (prevention, diagnosis, or treatment), on the area of specialty, and on the years of experience.

Table 3.9: Score statistics for Type 3 GEE analysis

Source	DF	Chi-Square	P>ChiSq
T	2	39.88	<0.0001*
S	4	11.85	0.0185*
E	1	6.47	0.0110*

* Significant at P<0.05

For fixed Specialty and years of experience, the conditional odds of a wrong answer to the prevention question are 10 times more as compared to the treatment question (Table 3.10). Similarly, the conditional odds of a wrong answer to the diagnosis questions are 2.56 times more as compared to the treatment question. Thus, given specialty and years of experience, participating physicians answered best on the treatment question, followed with the diagnosis question, then with the prevention question.

Table 3.10: Conditional Odds Ratio (OR) of incorrect answers to the three questions

Correct Answer	OR	C.I.
Prevention% Treatment	10*	(4.76; 21.7)
Diagnosis % Treatment	2.56*	(1.38; 5)
Prevention% Diagnosis	3.86*	(2; 8.33)

* Significant at P<0.05

For fixed years of experience and for a specific question, the conditional odds of responding right is 6.98 times higher in Rheum + Endo as compared to the baseline ObGyn; 4.24 times higher in IM as compared to the baseline; 4.06 times higher in FP+NP as compared to the baseline; and 3.74 times more in Ortho+Others as compared to the baseline ObGyn (Table 3.11). Thus, given the years of experience and the question asked, the knowledge about osteoporosis management went in a descending order from ‘Rheum + Endo’ to ‘IM’ to ‘FP + NP’ to ‘Ortho + Others’ to ‘ObGyn’.

Table 3.11: Conditional Odds Ratio (OR) of correct answers based on area of specialty as compared to the baseline (ObGyn)

Correct Answer compared to baseline (ObGyn)	OR*	C.I.
Rheum + Endo	6.98*	(2.4; 22.8)
IM	4.24*	(1.76; 10.19)
FP+ NP	4.06*	(1.53;10.8)
Ortho + Others	3.74*	(1.3; 10.72)

* Significant at P<0.05; Rheum=Rheumatologist; Endo=Endocrinologists; IM=Internal Medicine; FP=Family Practitioner; NP=Nurse Practitioner; Ortho=Orthopedics.

For fixed area of specialty and for a specific question, the conditional odds ratio of responding right is 4% higher as years of experience increases by one unit (Table 3.12). Thus, given the area of specialty and the question asked, the knowledge of osteoporosis increased as the number of years of experience increased.

Table 3.12: Conditional Odds Ratio (OR) of correct answers based on years of experience

Correct Answer	OR*	C.I.
(Year+1) % (Year)	1.04*	(1.014; 1.071)

* Significant at P<0.05

3.4. Discussion

3.4.1. Osteoporosis Prevention

The majority of the respondents (98%) prescribed a high calcium diet as well as exercise as a preventive measure before osteoporosis occurs (Table 3.3). 19% of the bone is made of calcium mineral and 99% of total body calcium is in the bones (Shils et al., 1998). Calcium is crucial for the formation and remodeling of bones as well as for calcium homeostasis. Vitamin D increases calcium absorption from the gut.

75% of the physicians would control for alcohol and smoking. Alcohol, if consumed in excess (>2cups/day), can directly affect direct bone tissue by inhibiting calcium absorption, and smoking decreases calcium absorption and the therapeutic effect of estrogen (Papazian, 1991).

Most of the physicians (55%) were reluctant about prescribing hormones as a preventive measure for osteoporosis in men and women who are hypogonadal (Table 3.3). According to specialty, the percentages of physicians were 44% of the IM, 27% of the ObGyn, 9% of the rheumatologists, and 9% of the family practitioners. However, it is known that sex steroids secreted in the body during puberty increase the bone mineral density (BMD) and the peak bone mass (NIH consensus, 2001). Thus any delay in the menarche (such as in strenuous exercise or under emotional stress or low body weight) will be reflected in the attainment of the peak bone

mass, and preventive measures such as prescribing gonadal steroids in this scenario are crucial to prevent osteoporosis. According to the literature, some studies have shown that hormone replacement therapy such as estrogens with or without progesterone can reduce the risk of hip fracture. Moreover, this reduction in the risk is proportional to the quantity and the duration of estrogen usage (Michaelsson et al., 1998). In a similar vein, Lindsay (1993) has favored the usage of hormone replacement therapy –estrogen, in addition to progestin only if the uterus was not removed- in order to prevent osteoporosis. Lindsay emphasized in his article the importance of patient monitoring; this includes bone mass measurement after 1 year of treatment, annual mammography, blood pressure measurement after 3 months of treatment, and lipoproteins profile because it is known that oral administration of estrogen increases HDL and decreased LDL (Barrett-Connor; 1993). In contrast, Minelli et al. (2004) have shown that the usage of hormone replacement therapy (HRT) as a prevention against osteoporosis in women without the menopausal symptoms is not recommended, namely in women with a baseline risk of breast cancer. Thus, the authors suggest an individualized approach tailored to the case of every individual in order to make a clinical decision. The WHO on the other hand recommends the use of HRT for prevention of osteoporosis in women with ovarian failure. The benefits of HRT outweigh their risks if given for a period of 10 years. It is important to inform women about the pros and the cons of HRT so to make an informed decision about its usage (WHO guidelines, 1994). On the other hand, the FDA recommends the minimum usage of HT for the shortest duration possible and with a minimum dosage only when other alternatives are not feasible (Stephenson, 2003); this is in congruence with NOF among other societies. Additionally, other evidence suggested that HRT was not recommended by FDA to treat osteoporosis (Lane et al.,

2003). These conflicting results are still reflected among the participants in the survey where only 45% of the physicians recommend HRT in hypogonadal patients.

Coffee intake in relation to osteoporosis was underestimated, where only 40% of the physicians were aware of the caffeine effect on calcium absorption (Table 3.3). Studies have shown that coffee intake has been associated with increased risk of hip fracture in elderly women (Kiel et al., 1990). This could be explained by the calciuretic effect of caffeine (Bergman et al., 1990) leading to a negative calcium balance (Hernandez-Avilla et al., 1991). However, Barrett-Connor et al (1994) have shown in their cohort study of 980 postmenopausal women that caffeine intake was associated with reduced BMD only in women who had marginal calcium intakes. Similarly, another longitudinal study found no association between caffeine intake and bone loss in postmenopausal women (Lloyd et al., 2000). Further studies comparing the timing of caffeine intake with milk or a few hours after milk consumption need to be conducted in order to understand the role of the timing of caffeine intake with respect to calcium.

3.4.2. Osteoporosis Diagnosis

The majority of the professionals who responded had indicated fracture as a risk factor for osteoporosis (Table 3.4a). This is concordant with previous data, which have shown that independent of bone mass, previous fractures of the spine are predictive of the risk of future spine fractures. One explanation may be that once a vertebra is damaged, it will change the mechanical loading on the remaining vertebrae, and thus make them susceptible to further fractures (Johnston and Slemenda, 1993).

Only 53% of the respondents considered low peak bone mass at early ages to be a sign of osteoporosis presence (Table 3.4a), while it has been suggested in 1984 that the peak bone mass reached in the third decade is “the most important factor that determines how much of the bone

will be lost before fractures occur” or a “low bone mass is reached” (Wahner et al., 1984).

Additionally, a 2-year randomized controlled trial in young women (20-35 years) showed that a combined regimen of aerobics and weight training had a positive effect on the BMD of the hip, spine, and calcaneus in the participants and thus on their peak bone mass (Friedlander et al., 1995).

Clearly, most physicians (90%) responding to the survey recommended the usage of Dual Energy X-Ray Absorptiometry (DXA) as a detection method before fractures occur (Table 4b), which is concordant with the WHO guidelines (1994) and with Marshall et al (1996) who declared that a DXA scan was a great predictor of fracture risk. However, only 29% of them recommend a DXA scan for all women above 65 years of age (Table 3.4c), although this is recommended by the guidelines set by both WHO and NOF. According to Morris et al. (2004), some of the barriers to BMD testing are the lack of uniformity in the content of the screening guidelines. Nevertheless, controversy exists among experts about whether BMD alone is enough as a diagnostic criterion (NIH consensus statement, 2000). Not only are there concerns about “region-specific reference ranges”, as well as “intra- and inter-manufacturer differences in hardware and software algorithms” (Formica, 1998), but also it is suggested that relying on just a single measurement of bone mass is an underestimation of the actual risk of fracture occurrence. In fact, previous low-trauma fractures may be indicative of a poor bone quality and are correlated with increased risk of fracture, independent of bone mass (Wasnich, 1993).

Appropriate referral of patients at risk is crucial for the optimal management of osteoporosis. This survey suggests that appropriate referral occurred in only 51% of the respondents who answered “yes” when asked if DXA should be used as a screening tool; however, 37% thought that DXA should be only for women at risk for osteoporosis because they

believed that BMD measurement was too expensive. 3% never considered DXA as a screening tool, most probably because they had no idea about who should have this procedure. 10% complained about the unavailability of a DXA machine at their facility, although they were aware of its importance as a diagnostic tool for osteoporosis. This should draw the attention of the health care community to make the DXA machine more accessible to the physicians at some hospitals. In fact, it has been shown in the literature that low-cost BMD screening is highly effective in motivating the patient in seeking medical consultation for osteoporosis prevention and treatment (Anastasopoulou and Rude; 2002); likewise, Cline et al. (2005) concluded from their cross sectional survey of postmenopausal women residing in Minnesota that BMD screening encourages the patient to engage in exercises (weight-bearing) and the physician to initiate a drug therapy. Recent evidence showed that if Medicare expanded by 10% the BMD testing for women for osteoporosis prevention, it could have saved billions (collated from Disease Management Advisor, 2003). On the other hand, according to the physicians' estimation, a mean of only 23% of patients would do the bone scan if they were not insured. All these current and previous findings corroborate the importance of a BMD screening; consequently, this should draw the attention of the health agencies to authorize this reimbursement.

Specifically striking is the fact that as many as 41% of the respondents suggested the usage of X-ray as a detection method before fractures occur (Table 3.4b), despite the fact that X-rays will only detect bone loss by the time $25 \pm 40\%$ of bone mass has already gone (Delmas, 1999). Herein, the lack of knowledge of some of the physicians is a problem towards a good osteoporosis management. Another deceiving fact was that only 43% of the physicians recommended a bone scan upon gluco-corticoid use (Table 3.4c), despite the fact that the NOF recommends a DXA scan in this particular scenario.

3.4.3. Osteoporosis Treatment

The majority of respondents had a global knowledge about osteoporosis treatment where all of them (100%) recommended calcium and most of them (89%) recommended vitamin D supplements as well (Table 3.5a). 95% of the respondents advised exercise. According to WHO, the effects of exercise on bone mass have been inconsistent; however, carefully designed exercises for women with osteoporosis have shown to optimize well-being, muscle strength, postural stability, and thus decrease the risk of subsequent fracture (WHO, 1994). While NOF recommends walking and resistance training for patients with osteoporosis, 85% of the respondents advised walking, and only 52% recommended resistance training (Table 3.5b). On the other hand, some studies have shown that swimming (Hart et al., 2001; O’Neil et al., 2002) increased bone density in OVX rats, but the effect on human is still controversial. In this survey, 33% of the respondents recommended swimming. Moreover, sports activities that include repetitive impact on the spine (running) may cause damage to the lumbar spine and are thus not favorable to people with osteoporosis (Shephard, 2002). Surprisingly, a few of the respondents demonstrated poor knowledge to the kind of exercise suitable for osteoporosis, where 20% recommended “running” and a few others recommended “non weight bearing activities” such as “bike riding”, albeit not recommended by NOF as a treatment for osteoporosis. In 1993, Heinonen et al. reported that the cyclist female athletes had relatively low lumbar and hip BMD when compared to other weight-bearing activities such as skiing or weight lifting. This may be explained by the fact that cycling does not include vertical weight-bearing activities. Sometimes, the nomenclature of the exercise regimens might be misleading to physicians and even to the patients themselves. There are a variety of non-weight bearing exercises that can be beneficial to osteopenia patients, as will be shown in Chapter IV, such as site-specific strengthening exercises

that target a specific area in the body, e.g. the lower back. These exercise can be beneficial to the bone mineral loss, although they are not all weight bearing or resistance exercises per se. Other longitudinal studies need to be done to test whether these type of exercises benefit patients who have osteoporosis, which is a more advanced stage in bone loss, as compared to osteopenia. On the other hand, other non-weight bearing exercises such as bike riding are known to be non beneficial for treating bone mineral loss. Consequently, physicians need to be more specific and consistent in prescribing exercises regimen to treat osteoporosis, by first increasing their knowledge about it, and by using a common nomenclature that does not confuse the patient. As for the physical therapy, 16% of the physicians answered “yes”. Their answer was considered correct, but more clarification needs to be mentioned about this technique. Emerging evidence has cautioned against the use of manual therapy in individuals with osteoporosis for fear of causing rib or vertebral fracture (Maitland et al., 2001). On the other hand, some physical therapists prescribe appropriate strengthening exercises when treating individuals with osteoporosis, which is considered a safe and adequate treatment.

As for exercise frequency, the majority of the respondents (58%) recommended a frequency of 3 times per week (Table 3.5c), and 61% reported a duration of 16-30 minutes each time (Table 3.5d). Although hormones were recommended by 45% of the respondents for osteoporosis prevention in hypogonadal patients (Table 3.3), 87% of the respondents recommended the usage of HRT as a treatment of osteoporosis (Table 3.5a), either estrogen alone (68%), or Evista (50%), or a combination of progesterone and estrogen (46%), or even testosterone (15%) as shown in Table 6e. The pros and cons of HRT in osteoporosis patients have been discussed above. To summarize those, we note that recent emerging evidence highlighted that the risks of long-term HRT in healthy postmenopausal women by far

outweighed the benefits in chronic health maintenance (Schulman et al., 2002); therefore, these substantial findings should prompt the cessation of its usage for this purpose. Additionally, it is important to note that most of the respondents recommended the usage of bisphosphonates (92%), with Fosamax being the favorite prescribed drug recommended by the physicians (90%), followed with Actonel (42%), then with Etidronate (15%). The issue of discussing what seems to be the best treatment for osteoporosis will be discussed in the next chapter (Chapter IV).

3.4.3.1. Best Treatment for Osteoporosis

No physicians recommended diet/supplements as the sole treatment for osteoporosis but 69% included diet/supplements in their combination treatment. The most commonly recommended treatment was the combination of diet/supplements + exercise + biphosphonates (44%) with some adding hormone replacement therapy or calcitonin to this combination. As a single best treatment, Biphosphonates was the first choice by 16% of the physicians.

According to the responding physicians, they considered that bisphosphonates would mostly improve BMD in 55.32% of the cases; second, hormones in 32.81% of the cases; third, calcitonin (18% of the cases), and last, diets and supplements (in 15.3 % of the cases) are recommended.

3.4.4. Osteoporosis Follow-up

Based on the physicians' estimation, 78% of the patients come back for a follow-up for another DXA every 1 to 2 years (Table 3.6). As for the rest, they either reported the unavailability of DXA, which should raise some red flags to the health authorities; or they said "every 3 to 4 years", which is too long of a period to follow-up with an osteoporosis patient; or they said "every 6 months", which is too short to show a change on the bone mineral density, taking into consideration the random error coming from the machine itself; or they said "never",

which is the worst case scenario for osteoporosis management. According to the literature, patients receiving HRT, calcitonin, or Selective Estrogen Receptor Modulator (SERM) should have a repeat BMD scan every 2 to 4 years; while patients receiving bisphosphonates should repeat it every 1 to 2 years (McGarry et al., 2003). In all cases, DXA scans should be more available to physicians in order to follow-up appropriately with osteoporosis patients, physicians should be aware that patients need to come back for a follow-up for another scan every 1 to 2 years. Conversely, Wei et al. (2004) reported in their paper that neither BMD nor bone turnover markers were substantially correlated to fracture rate reduction; consequently, the best optimal way to monitor a treatment efficacy remains unknown. Nevertheless, physicians should put more effort into explaining to the patients the importance and the seriousness of the disease and its follow-up in order to enhance patient compliance. Chapter IV will show the low percentage of patients' adherence to physicians' prescription; interestingly, 88% of the physicians are fully aware that the patients do not fully comply with their prescription (Table 3.7). This being said, physicians do need to take serious and sustained steps and be more involved in optimizing the management of patients with osteoporosis to enhance their compliance.

3.4.5. Comparative Analysis Discussion

Physicians' knowledge about osteoporosis management varied with the type of question answered. Physicians answered best on the treatment question, followed by the diagnosis, and then by the prevention question. It also turned out that rheumatologists and endocrinologists scored the best as compared to other specialties. This might be due to the fact that rheumatologists are more specialized in diseases related to the bones and the joints, and they deal with elderly people most of their time. Similarly, endocrinologists deal most of the time with the hormonal problems, which are very linked to the osteoporosis in post-menopausal women.

According to the WHO published summary, it is recognized that several medical specialties deal with osteoporosis patients; including “rheumatology, orthopedics, general practice, endocrinology, metabolic medicine, geriatrics, and obstetrics and gynecology”. These specialties deal with osteoporosis, albeit they are not equally “professionally trained” in metabolic bone diseases. This should draw the attention of the “relevant Royal Medical Colleges” and encourage them to include the osteoporosis management as a training component to all the relevant disciplines (WHO, 1994). In addition, it appeared that physicians with more years of experience scored higher in general. This might also be due to the fact that some of the respondents were residents (1 or 2 years of experience), and thus they are not expected to know as many details as physicians who were specialized in this field and with more years of experience.

3.4.6. Limitations

Knowing that physicians are a very busy population, they barely have time to read and fill out a questionnaire. Therefore, the response rate was not very high (25.2%); and thus the sample size was not fully representative of the target population of physicians. There may also have been a sampling bias where only physicians interested in osteoporosis filled the questionnaire. Another limitation is that there were a couple of questions in the questionnaire that were not very clearly understood by the respondents, and thus, they would skip the answer. This has lead to some missing values in some of the variables. Therefore, the summary statistics should be interpreted with caution, taking into consideration the sampling errors and the measurement errors.

3.5. Conclusion

Respondents displayed poor knowledge regarding osteoporosis prevention with gonadal steroids in hypogonadal patients; control of caffeine intake because of its calciuretic effect; osteoporosis diagnosis with X-rays; DXA scan recommendation upon glucocorticoid use; DXA scan recommendation for all women above 65 years of age; and the appropriate kind of exercise for osteoporosis treatment. Rheumatologists and endocrinologists scored globally better on osteoporosis management. Physicians with more years of experience were more knowledgeable of osteoporosis care.

3.6. Recommendations

There is a need to equally expand the knowledge among physicians with different areas of specialties, who deal with osteoporosis patients in Baton Rouge and New Orleans, with respect to prevention, diagnosis, and treatment of osteoporosis. Physicians need to convey the osteoporosis message to the patients in a sustained way that will improve adherence to the regimen. The health agencies should recognize DXA scan reimbursement and broaden its policy. There is clearly a need for greater availability of the diagnostic tool (DXA machine) in more hospitals in Louisiana. This will improve the standard care of osteoporosis and thus result in long-term significant savings to the government.

3.7. References

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CHAPTER IV

OSTEOPOROSIS TREATMENT AND PATIENT ADHERENCE: A CASE-REFERENT STUDY OF POST-MENOPAUSAL WOMEN IN BATON ROUGE

4.1. Introduction

Prior to 1990, estrogens and calcitonin (a thyroid hormone; injectible form) were the only two drugs authorized by the Food and Drug Administration (FDA) for osteoporosis treatment. Postmenopausal women were reluctant to use estrogen due to the concern about the continuation of their menstruation cycle, as well as the connection of estrogen to breast cancer (Papazian, 1991).

The major inconvenience of salmon calcitonin (injectible) is its cost: it is 10 times more expensive than estrogen therapy (Watts, 1994). On the other hand, nasal calcitonin has shown to decrease vertebral fracture frequency (WHO, 1994), albeit some unfavorable reactions such as nasal discomfort, nausea, and flushing were shown (Eastell, 1998; Watts, 1994).

For women diagnosed with osteoporosis, newer drugs such as bisphosphonates alendronate (Fosamax) and risedronate (Actonel) can help strengthen bone and prevent subsequent bone loss (Siris et al., 2004). Yet, the use of bisphosphonates is not recommended in individuals with hypocalcemia, persons with esophagus complications, and people who are unable to sit or stand for 30 minutes after each dose (McCoy, 2001).

Other varieties of new medications include the selective estrogen receptor modulator (SERM) Raloxifene (Evista) and more recently, intermittent parathyroid hormone (PTH) (Forteo). Although there has been a debate in the literature about whether pharmacological treatments can actually suppress bone resorption or add up bones, PTH was shown to add bone instead of just reducing the rate of bone loss (Siris et al., 2004).

Calcium alone may be partly effective in decreasing the rate of bone loss, particularly in elderly women and those who are deficient in calcium. Vitamin D increases calcium absorption, which may lead to beneficial effects on the bone (Eastell, 1998).

Because the number of treatment options is escalating, the decision-making process is becoming a hard task. There is even some controversy regarding the active treatment of osteoporosis (Speroff, 1999). According to Speroff, the ideal treatment for early postmenopausal women is hormone therapy. However, it is questionable that this applies to all post-menopausal women. Moreover, a lot of studies have looked into the different treatment approaches for management of osteoporosis; yet, none of the studies have looked into the patient's adherence to treatment protocol. So, does optimal osteoporosis management lie in the type of treatment prescribed or in the patient adherence to the treatment protocol?

4.1.1. Purpose

The goal of this study was to investigate the types of interventions for osteopenia/osteoporosis offered to a population-based case-referent of postmenopausal women with osteopenia/osteoporosis, and then to look at the outcome of these methods, including patient adherence to the treatment protocol.

The objectives were to answer the following questions:

- 1- Are patients compliant with the physician's prescribed treatment? If not, what are the barriers to compliance?
- 2- Based on the treatment followed, what kind of response is seen on the patients upon the second/third year of treatment? What is the best treatment for osteoporosis in practice? Does the treatment work equally on the spine and the femur?

3- Does optimal osteoporosis management lie exclusively on patient adherence?

4.2. Materials and Methods

Study Design: This study used a case-referent design. In a case-referent study design, “a series of people with and another without the illness are enrolled and their profiles with respect to the exposure, past or present, are ascertained and compared. The same population that gives rise to the case-series, gives rise to the referent series. The referent series are not people without the condition, but they are a sample of the population from which the cases came” (Olli Miettinen, 1976). The study consisted of 223 postmenopausal women who suffered from low bone mineral density in the femur, the spine, or in both.

Target population: Post-menopausal women, diagnosed with osteopenia or osteoporosis, who had followed a prescribed treatment for osteoporosis along with two dual-energy X-ray absorptiometry (DXA) bone scans taken within a time frame of three years prior to the time of the study.

Sample size: A total of 223 medical records were examined for this study.

Case series: Post-menopausal women who showed a positive response to treatment. This was determined by comparing the two DXA scans taken within the 3-year time frame. 1. The first DXA scan should show a BMD at least 1 SD below the mean. 2. The second DXA scan should show an increase in the bone density with respect to the previous measurement. 3. The case-series should be free from evidence of deterioration of bones for the previous 3 years of the study.

Referent series: They are women who showed no response to treatment. This was determined as follows: 1. The first DXA scan should show a BMD at least 1 SD below the mean. 2. The second DXA scan should show a decrease in the bone density. 3. Referent-series are

women who showed any of the following end-points: fractures, loss of height, curvature of spine, rounding of the back, falls, and broken bones during the study timeline.

Measurement of exposures, and covariates: In this study, subjects may have been exposed to different treatments for different periods of time within the 3-year time frame of the study. For the purpose of this study, a cut-off point of 1 year was set to classify subjects as exposed or non-exposed.

Data collection methods: Medical records of the subjects were reviewed for demographic data (age, race), behavioral data (cigarette smoking, alcohol use, exercise habits), allergies, history of present illness, past medical history, medications taken, family medical history, social history, and a variety of clinical information including review of systems (chest, breath, thyroid problems, diabetes, allergy, abdominal problems), physical examination results, and all medical correspondence with each patient. Record reviews were restricted to all post-menopausal women aged 45 years or older. Physician comments were followed gathering information on specific recommendations for osteoporosis interventions including medications and referral for BMD testing. Bone densitometry measurements were made using DXA scans.

An attempt to obtain information not available from the medical records was done through a patient phone interview; however only a subsample of 100 randomly selected patients was interviewed. Patients were called over the phone from Ochsner clinic. The Ochsner's Institutional Review Board for the protection of human subjects reviewed/approved the telephone script that was used for the study. A formal verbal consent of the patients to have access to this information was obtained. This information included actual treatment followed (adherence), the length of time of the treatment followed, as well as current assessment of exercise habits. Please refer to the attached script (Appendix 3) used for telephone interviews.

Inclusion criteria: Post-menopausal women diagnosed with osteoporosis or osteopenia in the femur and/or the spine area, and who have had at least two DXA scans within the previous 3 years. Some of the women should be accessible at the time of the study. Verbal informed consent was obtained prior to subject subscription for the interview.

Exclusion criteria: Women who were unreachable at the time of the study for medical reasons (death) or geographical reasons (migration) were not included in the sample size that was randomly selected to check about patient adherence.

4.2.1. Statistical Methods

A descriptive comparison between the physician prescription (obtained from the medical records) and what the patient said (obtained from the interview) was done to estimate the percentage of adherence and identify the barriers for non-compliance. Analysis of variance was used to test if the treatment means were equal in the spine and the femur areas. A Chi-square analysis (X^2) was done to estimate the odds of recovery while being on bisphosphonates in each site. Repeated Measures Anova using Proc Mixed was used to test if the treatment was consistent for both sites femur and spine, taking into consideration the repeated measures in space on the same subject as one variable “site”. To avoid complexity of the model, only the two-way interactions were kept in the model. Higher order interactions have lead to empty cell sizes and have made the analysis unable to run. Logistic regression using Proc Genmod was used to compare between the different treatments’ combinations that were followed. Ultimately, a modeling approach using a regression analysis with backward elimination was used to control for the different confounding variables and estimate their correlation with the change in bone mineral density in the spine and the femur. Only the main effects without any interaction were used in the model. All the confounding variables such as such as smoking, exercise, body mass

index (BMI), steroid therapy, history of osteoporotic fractures, genetics, milk intolerance, and illnesses such as cancer, thyroid disease, kidney failure, liver disease, and bowel disease were controlled for by including the significant variables in the model and removing the non significant variables. The statistical analyses were done using SAS (version 9).

4.3. Results

Two hundred and twenty three medical records were reviewed (Table 4.1). The subjects included had a low bone mineral density in either the spine or the femur or both. Of these 223 subjects, some of them had a low BMD in the spine only, others had a low BMD in the femur only, and others had low BMD in both areas. For the purpose of this study, we will first do a separate analysis for each of the spine and the femur. Among the 223 subjects, 208 subjects (143 cases and 65 referents) had a low bone mineral density in the spine and 201 subjects (107 cases and 94 referents) had a low bone mineral density in the femur (Table 4.1), knowing that some of the subjects in both groups are the same because they have low BMD in both areas. The mean BMI was in the range of 24 to 25 kg/m². The majority of the sampled women with low bone mineral density were Caucasian. When a sample of 100 women was interviewed over the phone, it appeared that only 37-38% was fully adhering to the physician's prescription, while 62-63% was partially adhering or not adhering at all.

Table 4.1: Descriptive characteristics of the study population

	Spine	Cases	Referents	Femur	Cases	Referents
Total (n=223)	208	143	65	201	107	94
Mean BMI	25.1± 5.2	25.52 ± 5.7	24.18 ± 3.8	24.6± 4.9	24.08 ± 4.7	25.18 ± 5.2
Race						
Caucasian	89%	87%	94%	91%	91%	90%
Others*	11%	13%	6%	9%	9%	10%
Adherence						
Yes	38%	42%	26%	37%	46%	29%
No†	62%	58%	74%	63%	54%	71%

*Others: Hispanic; African American; Native American; †Includes “partially” and “not at all”; BMI= Body Mass Index.

Table 4.2 shows the number of subjects who became cases (recovery from the disease) or controls (no recovery from the disease) in each of the femur and the spine. The percentage of people who recovered in the spine area (68.75%) was higher than in the femur area (53.23%) suggesting that the spine area is more responsive to the treatment. When the last DXA scan was assessed, it turned out that more women had osteoporosis in the spine (59%) and osteopenia in the femur (54.5%) suggesting that the spine was the area that was most susceptible to lose bone mineral mass. These results are also confirmed with the percentage mean changes in BMD in each area. The yearly change in BMD can go as low as -6.28 or -6.09 in each of the femur and spine respectively, and as high as 6.5 or 13.9 in each of the mentioned areas respectively. Here again the mean change per year in BMD was higher in the spine area.

Table 4.2: Descriptive characteristics at the end of the study

	Femur	Spine
N	201	208
% Case	53%	69%
% Referents	47%	31%
Normal (at the end)	0.5%	1%
Osteopenia (at the end)	54.5%	40%
Osteoporosis (at the end)	45%	59%
ΔBMD*/yr min	-6.288	-6.09
max	+6.521	+13.911
mean ± SD	0.23± 1.82	1.11± 2.56

*** Change in Bone Mineral Density (BMD) per year in g/cm²**

The subjects were on different kinds of treatments, whether a single treatment (e.g., dietary supplements, antacids, fosamax, actonel, evista, fortero, premarin, calcitonin, exercise), or a combination of two, three, or four treatments of the ones previously mentioned (Table 4.3). The number of subjects per treatment followed varied between a minimum of two and a maximum of 29 subjects. For the purpose of the analysis, treatments were collapsed into for

single groups (Fig4.1) such as “Calcium” (calcium and vitamin D supplements; or one multivitamin and one antacid); “Bisphosphonates” (fosamax; actonel); “Hormones” (premarin; evista; fortero; calcitonin); and “Exercise” or a combination of 2; 3; or 4 of these single groups. Note that the majority of the subjects who were taking bisphosphonates were taking mostly fosamax, and those who were on hormones were mostly on premarin (estrogen); nevertheless, to avoid bias, the broader name was chosen to indicate treatment groups.

Table 4.3: Mean yearly change in lumbar BMD and number of subjects per treatment followed

Treatment	N	Mean spine BMD \pm SD
B	3	8.64 \pm 6.85
BE	2	3.72 \pm 1.60
CaBE	29	2.17 \pm 2.85
CaBH	13	1.97 \pm 2.57
CaBHE	15	1.92 \pm 1.89
CaB	23	1.61 \pm 2.06
BH	2	1.59 \pm 0.84
H	7	1.51 \pm 1.44
CaHE	22	1.09 \pm 1.92
CaH	29	0.65 \pm 1.74
Ca	29	0.53 \pm 2.29
E	3	-0.04 \pm 3.08
CaE	28	-0.17 \pm 2.32
HE	3	-0.89 \pm 1.26

Ca=Calcium; B=Bisphosphonates (Fosamax/Actonel); H=Hormones (Premarin; Evista; Fortero; Calcitonin); E=Exercise; CaB =Calcium + Bisphosphonates etc...;

Analysis of Variance (ANOVA) of the mean yearly change in BMD in the femur showed that subjects who were on BH; B; CaBH; CaBHE; CaBE; BE; CaB; CaH; or H had higher increasing values of BMD as compared to CaHE; Ca; CaE; E; or HE, albeit these former were not significantly different among each other. Note that the bar graphs in Fig.4.1 with the same letter are not significantly different. It is also important to note that the ANOVA is unbalanced and the cells do not have equal size. Numerically, the treatment group of BH scored the highest increase per year in femur BMD but there was only one subject in that group. These results

should be discussed with caution. Subjects who were on either calcium alone, or calcium and exercise, or exercise alone, or hormone and exercise showed a decrease in femur bone mineral density. When comparing subjects who were on bisphosphonates vs. those who were not, the odds of recovery in the femur area (or being a case) was 2.08 times more in subjects taking bisphosphonates either alone or in combination with other therapies ($X^2=5.29$; $P=0.02$; $OR=2.08$).

Table 4.4 represents the mean yearly change in the femur BMD as well as the cell size per treatment followed. There was only one subject under the treatment combination of bisphosphonate and hormone. Analysis of variance of the mean change in BMD in the spine showed that subjects who were on Bisphosphonates had a significantly highest increase in spine BMD as compared to the rest of the treatment combinations (Fig4.2). Subjects who were on either exercise alone, or calcium and exercise, or hormone and exercise showed a decrease in spine bone mineral density. Chi-square analysis revealed that the odds of recovery in the spine area (or being a case) was 1.96 times more in subjects taking bisphosphonates either alone or in combination with other therapies ($X^2=5.28$; $P=0.02$; $OR=1.96$).

When the variables (femur and spine) were combined into one variable (site), repeated measures ANOVA was used to compare if both sites reacted similarly to the treatments followed, and to test which treatment appeared to have an overall increasing effect on the bone. Table 4.5a displays the significant main effects and interactions obtained from the repeated measures ANOVA.

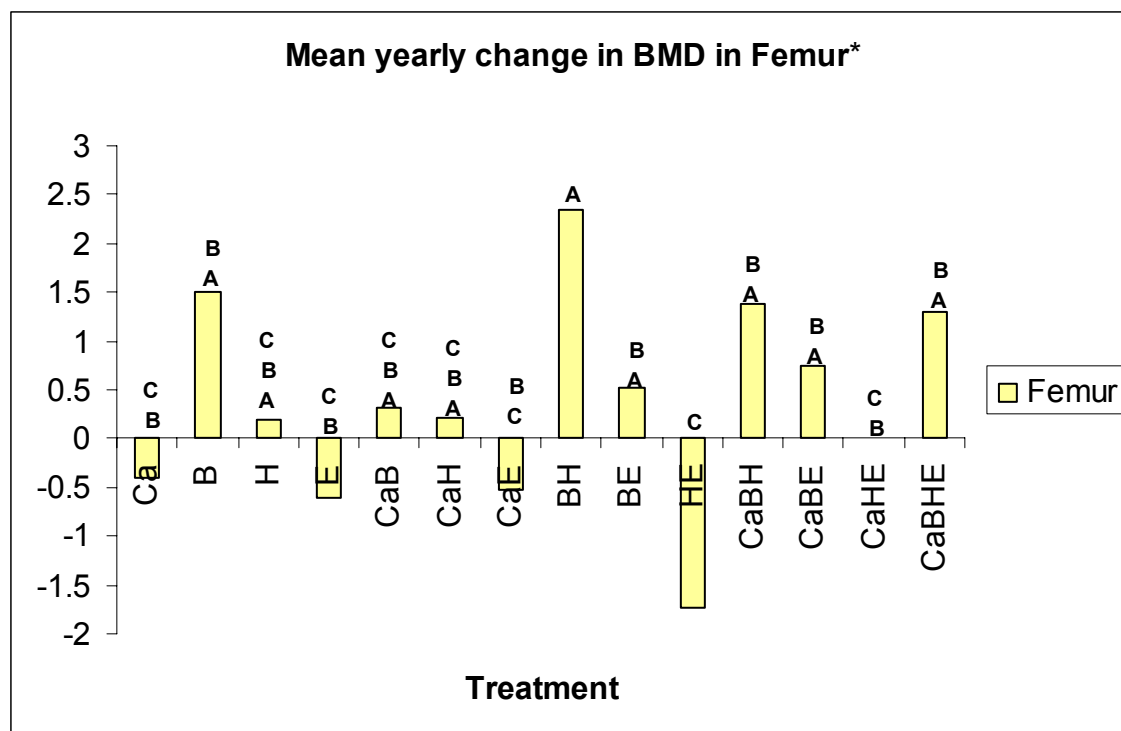


Fig. 4.1: Mean yearly change in BMD in the femur according to different treatment combinations
***Means with the same letter (A; B; or C) are not statistically different.**

Table 4.4: Mean yearly change in femur BMD and number of subjects per treatment followed

Treatment	N	Mean femur BMD \pm SD
BH	1	2.35 \pm .
B	3	1.49 \pm 0.79
CaBH	13	1.37 \pm 2.02
CaBHE	14	1.24 \pm 1.28
CaBE	27	0.80 \pm 1.49
BE	2	0.52 \pm 1.68
CaB	21	0.30 \pm 2.01
CaH	27	0.21 \pm 1.89
H	9	0.19 \pm 1.15
CaHE	23	0.07 \pm 1.63
Ca	28	-0.40 \pm 2.15
CaE	25	-0.56 \pm 1.30
E	5	-0.6 \pm 1.52
HE	3	-1.72 \pm 3.37

Ca=Calcium; B=Bisphosphonates (Fosamax/Actonel); H=Hormones (Premarin; Evista; Fortero; Calcitonin); E=Exercise; CaB =Calcium + Bisphosphonates etc;

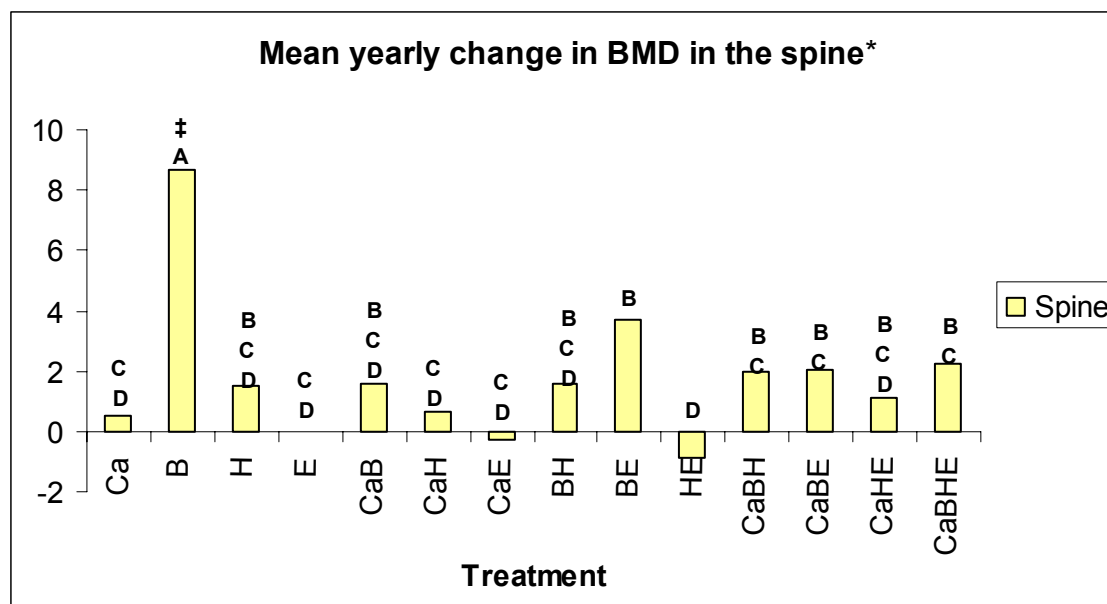


Fig. 4.2: Mean yearly change in BMD in the spine according to different treatment combinations
***Means with the same letter are not statistically different; ‡ Bisphosphonates had significantly the highest mean yearly change in BMD in the spine**

Table 4.5b shows in more details where this significance comes into play; it indicates that the spine showed more response to the treatment than the femur; this can be also seen in Fig4.3 below, where the mean yearly change in BMD was higher in the spine as compared to the femur, for almost all the treatment protocols followed. Fig4.1 and Fig4.2 are both depicted in Fig4.3.

Table 4.5a: Repeated measures ANOVA with two-ways interactions

Type 3 tests for fixed effects		
Effect	F value	Pr>F†
Site	28.35	<0.0001
Site*Calcium	4.15	0.04
Bisphosphonates	8.45	0.005
Exercise	7.04	0.01
Ca*Exercise	8.86	0.0031
Ca*Hormones	7.63	0.008

† Only significant results were reported

In addition, Table 4.5b shows that calcium acted better in the spine than on the femur; Moreover, it also appeared that being on bisphosphonates was better than not being on them, yet, exercising alone was not statistically different from not exercising; being on calcium alone was

worse than being on a combination of calcium and exercise, or calcium and hormones, or even on hormones alone.

Table 4.5b: Repeated measures ANOVA: significant main effects and interactions

Method=Tukey-Kramer (P<0.01)	LSMeans	Letter group†
Spine	1.80 ± 0.25	A
Femur	0.38 ± 0.25	B
Spine*Calcium	1.24 ± 0.17	AB
Femur*Calcium	0.36 ± 0.17	C
Bisphosphonates	1.79 ± 0.37	A
No Bisphosphonates	0.38 ± 0.27	B
Exercise	0.47 ± 0.34	A
No Exercise	1.7 ± 0.29	A
Ca*Exercise	0.88 ± 0.2	AB
Ca	0.72 ± 0.2	B
Ex	0.07 ± 0.64	AB
Ca*Hormones	1.03 ± 0.21	AB
Ca	0.57 ± 0.19	B
Hormones	0.29 ± 0.67	AB

†Means with the same letter are not statistically different; A is better than B; B is better than C; AB is better than B; AB is better than C.

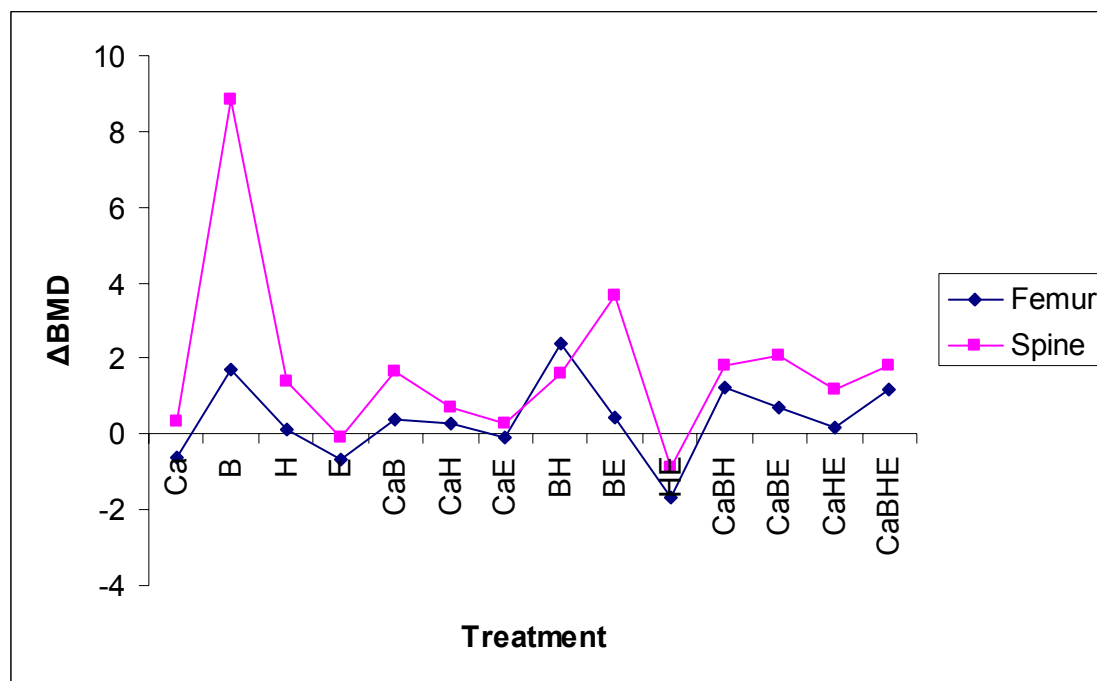


Fig. 4.3: Mean yearly change in BMD in Femur & Spine vs. Treatment

Taking the subjects who were just on calcium as a baseline (Table 4.6), the logistic regression analysis showed that the odds of recovery while being on CaBHE is 5.68 times the odds of being on just Ca for the spine. As for the rest of the combinations, no significant difference was seen among the treatments.

Table 4.6: Logistic regression results for the spine comparing the odds of being on CaBHE vs. being on Ca

Analysis of Parameter Estimates					
Parameter	DF	Estimate	OR	Wald X^2	P> X^2
Intercept	1	0.2076	-----	0.31	0.5782
CaBHE	1	1.7383	5.68	3.87	0.039*
Ca	1	0.00	-----	.	.

*Significant at P<0.05

Table 4.7 displays the significant odds ratio of the different treatments in the femur. The analysis showed that odds of recovery while being on CaBE were 3.16 times the odds of being on just Ca in the femur. Similarly, the odds of recovery while being on CaBHE were 5.33 times that of being on just Ca. In addition, the odds of recovery while being on CaBHE were 1.68 times than being on just CaBE (OR=1.68), however, this synergistic effect of the hormones was not significant CI= (0.3; 7.05).

Table 4.7: Logistic regression results for the femur comparing the odds of being on CaBHE vs. being on Ca and the odds of being in CaBE vs. being on Ca

Analysis of Parameter Estimates					
Parameter	DF	Estimate	OR	Wald X^2	P> X^2
Intercept	1	-0.2877	-----	0.57	0.4513
CaBE	1	1.1527	3.16	4.11	0.04*
CaBHE	1	1.674	5.33	4.42	0.025*
Ca	1	0.00	-----	.	.

*Significant at P<0.05

Another modeling approach was tried in order to control for the different confounding variables and to include them in the analysis. Table 4.8 shows the results of the stepwise regression with backward elimination procedure. The variables that were eliminated were

illnesses, smoking, milk intolerance, exercise, and steroid. As for the remaining variables, they were significant at the 0.1 level or the 0.05 level as the table indicates.

Table 4.8: Summary of stepwise regression with backward elimination showing the significant correlation of the variables with the change in BMD

Variable†	Parameter Estimate	Standard Error	Type II SS	F value	Pr>F
BMI*	0.04496	0.02090	20.55778	4.63	0.0321
Genetics	-0.40889	0.22942	14.10733	3.18	0.0755
HistFx	-0.39983	0.21844	14.87897	3.35	0.0680
Site*	-0.96684	0.21363	90.96672	20.48	<.0001
Ca	-0.58356	0.34666	12.58528	2.83	0.0931
B*	1.62289	0.22508	230.88011	51.99	<.0001
H	0.36350	0.21848	12.29339	2.77	0.0970

†All variables kept in the model are significant at the 0.1 level; * P<0.05; BMI=Body Mass Index; HistFx= History of fractures; Ca=Calcium; B=Bisphosphonate; H=Hormones;

It appeared that BMI, bisphosphonates, and hormones had a positive slope. This suggests a positive correlation between these variables and the change in BMD. As for the remaining variables such as genetics, history of fractures, and calcium taken alone, these had a negative slope. This suggests a negative correlation between these variables and the change in BMD. “Site” was coded as a binary indicator 0 or 1, with 0 referring to spine and 1 referring to femur. The negative slope obtained for “site” simply indicates that the change in BMD is less in the femur as compared to spine.

Table 4.9 shows barriers to adherence to the various treatments prescribed by the physicians. For calcium and vitamin D supplements, some women complained about stomach bloating and constipation problems. For bisphosphonates, the identified barriers were cost, rash, digestive problems for “fosamax” and intolerance for “actonel”. For hormones, the main barriers were the risk of cancer, the continuation of menstruation, and the indecision among physicians for use of premarin, and the cost of “evista”. As for the recommendations of exercise or smoking cessation, the barriers were lack of motivation and will from the patients to do so.

Table 4.9: Barriers towards subjects' compliance

Non Adherence to:	Causes
Calcium + vitamin D	✓ Stomach bloating/problems; ✓ Constipation
Exercise	✓ No motivation; No will
Fosamax	✓ Cost; ✓ Digestion, stomach, esophagus, swallowing problems; Diarrhea; ✓ Rash; ✓ "Not know about it".
Actonel	✓ "can't tolerate"
Evista	✓ Cost
Hormones (Premarin)	✓ Ovarian/ colon cancer risk; ✓ Menstruation; ✓ Indecision among physicians
Smoking cessation	✓ No motivation; no will

4.4. Discussion

Dietary factors such as calcium intake in childhood, adolescence, and later in life, estimate intake of salt, caffeine, and alcohol; smoking; physical activity in childhood and adolescence; age at menopause (premature menopause); amenorrhea; small skeletal frame, low BMI, steroid therapy, history of osteoporotic fractures, illnesses such as cancer, thyroid disease, kidney failure, liver disease, and bowel disease might affect the development of osteoporosis later in life" (Goldmann and Horowitz, 2000). Thus, these variables might bias our results in comparing groups that might be different inherently for reasons other than the treatment or "exposure" factor. Getting the information from the medical records before hand is one way of controlling these confounding variables. However, variables such as previous calcium intake and exercise habits since childhood will be assumed to have a diluted effect for the three years time frame of the study. In practice, it is hard to collect such detailed information related to childhood lifestyle habits from the medical records or even from interviewing the women themselves.

Sixty two to 63% of the phone interviewed patients did not partially or fully adhere to the prescribed regimen. Among the remaining 38% who adhered, they adhered mostly to the combination of calcium, exercise, and bisphosphonates. This being said, the reality was not far away from the physicians' estimation as shown in chapter III, where 88% of the surveyed physicians thought that the patients did not partially (87%) or fully (1%) follow their prescription. The result of this case referent study suggests that osteoporosis management depends to a certain extent on patient adherence. The survey conducted in chapter III suggests on the other hand that osteoporosis management relies in the treatment prescription or the physician's knowledge about it per se. Adding these two studies together, the answer will be that osteoporosis management relies on both factors: patient adherence and treatment prescription.

The spine was more responsive to treatment than the femur area (Fig4.3). It also showed that not only were there more subjects who recovered from the disease in the spine as compared to the femur, but also there were more people who had more osteoporosis in the spine than the femur in their most current DXA scan. This suggests that the spine area is a more susceptible area for bone turnover, and it is also more sensitive to treatment. One possible explanation behind this mechanism might be a regression towards the mean, where the weaker area is the one that shows more improvement. This finding is consistent with previous findings where it was stated that the femur and the spine are two different types of bone. The femur is predominantly cortical "appendicular skeleton" and the vertebra is predominantly trabecular "axial skeleton". There is a differential bone loss not only between the two kinds of bone, but also among different trabecular bone sites (Wahner et al., 1984). It was also suggested that the vertebral trabecular sites were more susceptible to bone loss and had a higher turnover rate as compared to other bone sites, whether cortical or non-vertebral trabecular sites. This might be due to the greater

surface area of the vertebra upon which osteoclasts can function (Lane et al., 2003) or the greater blood supply towards the trabecular bone surfaces because of its proximity to the bone marrow (Mazess, 1983). As far as the different responses seen among patients, the yearly percent change in BMD in both areas varied from negative to positive. In other words, the kind of response upon a treatment can be a decrease, maintenance, or an increase in BMD. According to Wilkin (1999), it is believed that an increase or maintenance in bone density with treatment is a good indication that treatment is effective. Similarly, according to Cooper (2000), osteoporosis cannot be eliminated, but the medications can slow down the bone turnover and rebuild some of the bone.

It appears that bisphosphonates and hormones or bisphosphonates therapy alone result in the highest mean response numerically, but it is not statistically different from B; H; CaB; CaH; BE; CaBH; CaBE; or CaBHE. These treatments have the same letter “A” on Fig4.1. Note that the analysis of variance that generated these results was unbalanced. For instance, there was only one subject that was under BH, and this subject had the highest numerical value in change in femoral BMD. Thus, conclusions should be drawn with reservation. Surprisingly, it appeared that bisphosphonates alone had the highest effect in the spine as compared to the rest of the treatments (Fig4.2). These results are similar to the findings Follin and Hansen (2003) where they suggested that when it came to pharmacological therapy, bisphosphonates showed the greatest benefit in bone loss prevention and fracture risk lowering. On the other hand, other studies were conducted to evaluate several combination therapies, but the results were conflicting. In some randomized controlled trials, combination therapy showed greater increases on BMD than either agent alone (Johnell et al., 2002) but the results on the fracture risk are still unknown. Further studies need to be implemented in order to test the validity of this

observation. The negative effects of CaE; E; HE in the femur and spine and Ca in the femur can be explained by three reasons. First, these negative numbers were not statistically different from other positive numbers observed under other treatments (as seen in the letters indicated on the bar graph in figures 4.1 and 4.2). Second, the target population chosen for this study was postmenopausal women who suffered from low bone mineral density, with the cut-off chosen being the one for osteopenia. Third, the design is unbalanced and the sample size is relatively small as compared to the myriad of combination treatments in the study. This being said, there were a number of subjects who started off with osteoporosis and if these patients were put on just calcium, or exercise, or calcium and exercise, they didn't show improvement in their bone mineral density. It appears that if the stage of the disease is advanced, patients need to be on an anti-resorptive therapy such as bisphosphonates. Yet, for postmenopausal women who have osteopenia, calcium and exercise alone might be enough to counterbalance the bone turnover. Congruent with our findings, Siris et al. (2004) stated that for osteopenia, non-pharmacologic treatments such as resistance training exercise and adequate calcium intake were advised to counterbalance the bone turnover. But in more advanced situations such as osteoporosis, an anti-resorptive therapy was needed to prevent fractures. It is important to explain why the target population was chosen to be patients who had the disease or the condition of low BMD; in chronic disease epidemiology, incident (new) rather than prevalent (already established) cases are enrolled. In case of a prevalent case (i.e. a person who responded to treatment before the 3 years time frame), one should be excluded from the computation of the population-time of experience, otherwise, it will be necessary to assume that the duration of illness (response to treatment) is unrelated to exposure. To avoid this dilemma, the recruited subjects were chosen in

a way they all had the disease, in this case, low bone mineral density in either femur, spine, or both.

The results of the repeated measure ANOVA confirm that the spine is more responsive to treatment as compared to the femur ($P < 0.01$) (Table 4.4b). This is also shown in fig4.3.

Exercise did not improve the BMD when compared to non exercise since exercise alone is not enough for people with advanced stage of the disease. The combination of calcium and exercise was more significant than calcium alone. This is congruent with the finding of Specker (1996) who concluded that calcium supplements can only be beneficial on bone health if complemented with adequate physical activity.

The combination of the four treatments of Ca, B, H, and E had higher odds of recovery from the disease as compared to being on one sole treatment such as calcium. However, when another mono-therapy is taken as a reference, the odds of recovery were not significantly different as compared to being on a combination of 2; 3; or 4 drugs. The literature regarding this matter has been conflicting. On one hand, some studies discouraged the use of combination therapy suggesting there is no substantial evidence to recommend such a treatment for osteoporosis (Compton and Watts, 2002); on the other hand, McGarry et al (2003) suggested that the combination of alendronate and raloxifene produced significantly higher gains than either drug alone. While table 4.6 suggests that adding hormones onto CaBE was not significantly any better than just CaBE, Eastell (1998) has likewise shown that there was no evidence that combining ERT onto bisphosphonates was more effective than either treatment alone. Due to the unbalanced design and the small cell size in some of the treatment combinations, there was surprisingly no significant difference among the remaining treatment combinations. The odds ratio in this case is an estimate of the incident-density ratio, “without

the need of the rare disease assumption' (main characteristic of the case-referent studies) (Miettinen, 1976). The incidence density ratio tells the risk of development of case (in this case recovery) in relation to the exposure (treatment followed) for various time periods. However, due to the complexity of the treatment combinations followed by patients, the unavailability of the exact information of the length of time under which they were following a certain treatment, and their recall bias even when they were verbally asked about the length of time they have been on a certain treatment, all these reasons have made the estimation of the exact time periods impossible to the estimation of the incident density ratio. To solve the problem of exposure or non exposure, a cut-off point of one year was chosen to define exposure to a specific treatment. This being said, the OR calculated in tables 4.5 and 4.6 are an estimation of the incident density ratio for an average of a one year period of time.

None of the analyses mentioned above were able to control for all the variables that are known to influence the response to the treatment. The stepwise regression (Table 4.7) eliminated the non-significant variables and kept the significant ones. Again, it appeared that the correlation between calcium alone and the change in BMD was negative. This might be explained by the same reasoning that calcium alone is not enough to compensate for the bone turnover at the advanced stage of the disease. Bisphosphonates showed the highest slope estimate, which is consistent with the literature. This analysis also confirms that spine is more responsive to treatment than femur because of the negative slope obtained for "site". The intake of hormones was positively correlated to an increase in BMD. BMI was positively correlated to the increase in BMD as well. It is possible that the heavier the body, the more weight the bones have to bear, and thus the stronger the bone density. Genetics and history of fractures were both negatively correlated to BMD. Studies have shown that if a previous fracture occurs, then it is more likely

that another one happens subsequently, independently of bone mass (Johnston and Slemenda, 1993).

A weight of evidence suggested that subjects who had suboptimal dietary calcium intake were the ones who reported higher barriers as compared to those receiving adequate amounts (Wallace, 2002) and subjects who reported lower barriers to exercise were the ones more likely to engage into a regular weight bearing exercise (Blalock et al., 1996). Table 4.9 displays the barriers to adherence as mentioned by the interviewed patients. Some of these barriers can be overcome by finding an array of medications or anti-resorptive therapy that can be tailored to different individuals with different tolerance levels. For instance, if some women cannot tolerate “fosamax”, they need to be switched to “actonel” or to another kind of treatment. On another note, the inconsistency among physicians about the usage of a certain therapy, say hormones, might lead the patients to confusion and might hinder their adherence. Moreover, congruent with the findings of the survey in chapter III, it is suggested that physicians need to be more involved into explaining to the patient about each treatment prescribed. Interestingly, Hsieh and coworkers (2001) reported that women who expressed worry about osteoporosis were more likely to adhere to hormone therapy, weight-bearing exercise, calcium or vitamin D supplements. This being said, physicians need to discuss with the patient the seriousness of the disease and how important it is to follow the prescribed regimen, whether it is exercise, or cessation of smoking, or any other behavior modification. In fact, studies have shown that although Americans might be aware of the exercise health benefits (Morrow et al., 1999), their behaviors indicate that they are probably unaware of how to become physically active to achieve a health benefit (Morrow et al., 2004). Behavior modification requires a lot of psychology, motivation,

education, and persistence from both sides; so it is the role of the physicians to play this role as much as possible to enhance positive feedback from the patient.

4.4.1. Limitations

The present study provided data from a 3 year population-based sample, with correlation to medical record information. This was done in order to minimize misclassification bias. The confounding variables such as previous dietary habits and exercise habits were considered as diluted within the 3 years time frame of the study.

Other sources of biases:

Selection bias: the establishment of the inclusion and exclusion criteria already created a selection bias. There is also a survival bias where only those who survived were included because it is a retrospective study. It is not known whether the cause of death of some patients was related to osteoporosis or to other reasons. Besides, the sampling frame for selecting cases and controls were restricted to one location. Thus, it is questionable whether the sample selected really represented the target population (cases of women outside the location of the study).

Misclassification bias: Recall bias; this is shown especially while interviewing the patients about their actual treatment followed and their current level of physical activity. However, to control for this source of bias with respect to the other variables and exposures, the duration of the study is confined to a period of 3 years.

The carry over effect of the medications that were taken within the previous six months prior to the time frame of the study and not during the study might affect the BMD changes.

4.5. Conclusion

Osteoporosis management relies partly on patient adherence. 62% of the patients didn't fully adhere to the prescribed regimen. Barriers to adherence varied from physiological reactions

to a specified treatment to a lack of motivation from the patient. Physicians need to be more involved in monitoring compliance. The change in BMD under a specific treatment can vary from a decrease, to maintenance, or to an increase in BMD, without necessarily achieving the normal BMD range. Spine, the area mostly affected, showed more improvement with treatment than the femur. Bisphosphonates acted best on the spine statistically and on the femur numerically. Combining calcium with exercise or calcium with hormones was better than either one alone, but may not be enough if the patient had osteoporosis. An anti-resorptive medication might be needed if the disease was advanced. Ultimately, low BMI, genetics, and history of fractures were negatively correlated to the increase in BMD. Thus, these risk factors for osteoporosis are also risk factors for further progression of the disease as seen by decreased BMD in this study.

4.6. Recommendations

Novel means of osteoporosis management should be approached by physicians to overcome the barriers for patients' adherence. Moreover, criteria for monitoring adherence should be established.

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CHAPTER V

THE EFFECT OF CALCIUM SUPPLEMENTS AND SITE-SPECIFIC STRENGTHENING EXERCISES ON LUMBAR MINERAL DENSITY AND MUSCLE STRENGTH IN OSTEOPENIC WOMEN: A ONE-YEAR PILOT STUDY

5.1. Introduction

There has been no general consensus with respect to the exact type and amount of exercise that would be beneficial to patients with osteoporosis (Watts, 1994; Henderson et al., 1998). Moreover, it is still not known whether bone in the elderly can be maintained with slightly above the average habitual activity or with some non-athletic exercises with low to moderate intensity levels (Kemmler et al., 2004). Walking 20 to 30 minutes three times per week (Watts, 1994) or walking 30 minutes daily in one to three bouts in addition to resistance training two times per week (Asikainen et al., 2004) has been suggested to be of a benefit. Any activities that might lead to falling need to be avoided (Watts, 1994).

Recently, researchers have focused on determining whether different forms of physical activities targeting critical skeletal sites can enhance the BMD in postmenopausal women. Generally speaking, the major muscle groups are easily targeted in everyday life (leg and arm muscles), yet at the expense of neglecting other areas in the body that need to be specifically targeted such as the lower back. Not only is this area often neglected in people, but also it can be damaged by some kind of repetitive impact activities (e.g. running) or weight lifting at the end of a range of motion (Shephard, 2002). Yet, a recent meta-analysis of randomized trials (15 studies) has shown that both impact (e.g. aerobics) and non-impact (e.g. weight-training) exercises had a positive impact on the lumbar spine mass in post-menopausal women (1.6% bone loss prevented vs. 1% bone loss prevented respectively) (Wallace and Cumming, 2000). According to Rutheford (1999), most studies do not detect a difference between the impact of

both types of exercises (endurance and strength training) on the lumbar mineral density. In all cases, however, the lower back along with the abdominal muscles should be targeted in every exercise activity, because they both represent the core of the body and they keep this last under balance and control (www.spine-health.com). In a similar vein, Sinaki et al. (1993) have emphasized the importance of assessing the safety and effectiveness of exercise programs designed to strengthen the lower back muscles and to improve the posture in postmenopausal women because of the higher vulnerability of the spinal trabecular bone to mineral loss as compared to other areas.

Moreover, recent researches have suggested that inactivity can be detrimental to the muscles of the lower back and it can lead to a longer recovery period or even worsen the condition. In 1991, Limburg et al. mentioned that weaknesses in the lower back muscle group (extensors and flexors) can lead to vertebral compression in people with osteoporosis in the spine. Similarly, in 1989, Sinaki noted that strengthening the back extensor muscles that are already weak can help in maintaining good posture and vertical alignment.

According to White (2001), osteopenia can be managed primarily by exercise and adequate nutrition; there is no evidence that a pharmacological treatment is needed at this stage. On the other hand, other literature negates the fact that a treatment for osteoporosis can actually restore bones, although (unlike calcium supplements) antiresorptive therapy has been shown to prevent bone resorption (Peel et al., 1995).

According to the American College of Sports Medicine guidelines (ACSM, 2000), “muscular strength is best achieved by the use of weights, but it can also be developed by static or dynamic exercises”; this means that muscular strength can be improved without using any external object for extra resistance.

In the literature, strength training has always been related to weights. In this study, however, no weights were involved due to the possibility that some people with bone problems might not be able to lift any weights. The site-specific strength exercises that were given only utilized the body weight of the subject. In fact, there has been some concern in the literature about the efficacy, practicality, safety, and compliance of elderly to resistance training, especially if they haven't had any previous experience in regular weight training (Petranick and Berg, 1997). It is also cumbersome for elderly to go to the gym or to be obliged to use some equipments for the long term.

This being said, the idea of developing a safe site-specific exercise program, easily accomplished by elderly people suffering from low bone density (T score <-1 SD) has emerged. These exercises target the core and lower back muscles attached to the lumbar spine, without using any extra weights or any instruments. In fact, Hsieh and Turner (2001) concluded from their interventional rat study that increasing load frequency can lead to osteogenesis. Home based exercises are becoming an attractive alternative to clinical therapies, knowing that the health care resources are limited (Hakkinen et al., 1999).

5.1.1. Purpose

The goal of the study was to design an appropriate, convenient, and inexpensive home exercise program for postmenopausal women suffering from low bone density. The program consisted of site-specific core/lower back strengthening exercises.

The primary objective was to prevent the accelerated bone loss induced by menopause via the core/lumbar strength exercises. Secondary objectives were to improve isometric lumbar strength and overall quality of life.

5.2. Materials and Methods

Study design: The experimental design was a pretest-posttest control group design.

Subjects and procedures: Medical records of postmenopausal women from Ochsner clinic were examined. Forty women who fit the criteria were contacted by phone by the investigator. They were verbally asked if they were interested in being a participant in the study. At first, 20 women showed interest and accordingly, they were mailed the informed consent form to be signed. Only 11 women returned the signed informed consent. They were then assigned appointments for measurements. Five women were in the exercise group and another 6 women were in the control group. However, one woman dropped out of the exercise group during the study for personal reasons unrelated to her physical skeletal health. The final sample size was 10 women. The 10 women gave their informed written consent before the testing and after all procedures were explained to them. All methods and procedures were approved by the Institutional Review Board of Ochsner Clinic Foundation in New Orleans. The treatment allocation was made by the participants' choice. The women in the exercise group were assigned the core/lower back strengthening exercises for a period of one year, 3 times a week, 40 minutes each time; The control group were either not active (2 subjects), or already involved in a physical activity such as weight lifting (n=1), walking (n=1), working in the yard (n=1), aerobics (n=1) but not doing the exercises designed for this pilot study. The women assigned to the control group were asked to maintain the same pattern of their dietary intake and physical activity throughout the study. Both groups were asked to attend the three meetings for isometric lower back strength measurement (pre, mid, and post study) and the two meetings for the Dual Energy X-ray Absorptiometry (DXA) scan measurements of the spine (L1-L4) (pre- and post study). All measurements were done by the same subjects on the same machines. All the women were on

calcium supplements except for two: one in the exercise group where her total daily calcium intake was 800 mg and another woman in the control group where her total daily calcium intake was 1000 mg. One subject who completed the study was excluded from the analysis due to her low calcium intake and high intake of synthroid, which would confound the results.

Inclusion criteria: Participants had to meet the following criteria to be enrolled in this study:

- Be psychosocially, mentally, and physically able to fully comply with the exercise protocol including adhering to the follow-up schedule and requirements and filling out forms.
- Have medical clearance to begin a physical exercise program.
- Provide a signed informed consent
- Be postmenopausal women, and do not exceed 75 years of age.
- Suffer from osteopenia: low bone density ($-2.5 \text{ SD} < \text{T score} < -1 \text{SD}$)
- Have a bone scan taken at the time of the beginning of the study or three months prior to the study.

Exclusion criteria: Women with the following criteria were excluded from the study:

- Osteoporosis, (if DXA bone density is less or equal to -2.5 (The World Health Organization definition of osteoporosis)
- Frail women above 75 years of age
- Morbid obesity defined as Body Mass Index (BMI) >40 or weight more than 100 lbs over ideal body weight.
- Systematic disease including AIDS, HIV, hepatitis.
- Back pain of unknown etiology
- Under hormonal replacement therapy

- Underweight women (BMI< 18.5)
- Previous hip or vertebral fracture (Fracture risk drastically increases following the first fracture, according to some literature (Watts, 1994).
- On daily steroids.
- Undergoing exercises different from the ones assessed at baseline.
- Contraindication to participation in back strength measurement and back exercises.
- Previous spinal operation
- Deficiency in calcium and vitamin D (<800 mg/day)

Data collection strategy: The data of the different variables were collected as follows:

- Height and weight and body mass index for all subjects were recorded
- Physical activity readiness for each participant will be identified by the Physical activity readiness questionnaire (PAR-Q) (Appendix 4) (www.csep.ca/pdfs/par-q.pdf)
- Level of physical activity. The participants were asked to complete the Aerobic Center Longitudinal Study Physical Activity Questionnaire (ACSM, 2005) at the beginning and at the end of the study to monitor changes. This Questionnaire is designed to conduct physical activity pattern, including leisure and household, during the past three months. Information regarding walking, stair climbing, jogging, swimming, weightlifting, aerobic dance, and household activities were acquired. All kinds of physical activity were accepted besides the specific core/lower back strengthening exercises (Appendix 5)
- Baseline calcium/vitamin D intake: Subjects were asked to complete a food frequency questionnaire focusing on the calcium rich, calcium rich food, high-protein foods, caffeine containing beverages, and alcoholic beverages food pre- and post-study to monitor calcium deficiency or changes if any (Appendix 6)

- Global health assessment variables were measured such as global strength, global pain, and a general well-being, using the short form 36 (www.swin.edu.au/victims/resources/assessment) pre- and post-study to monitor any changes in the feelings of well-being (Appendix 7)
- Medical history and health related behaviors were measured using the health status questionnaire (www.ncsf.org/pdf/downloads/Health_Status_Questionnaire) (Appendix 8)
- BMD: Lumbar BMD determined by DXA (GE Lunar Prodigy ^a) was assessed at baseline and at the end of the study (gemedicalsystems.com). All subjects were measured on the same DXA by the same technician (D.K.)
- Muscle strength: Isometric strength of back extensor muscles were measured at different joint angles (0; 12; and 24) using a back isometric dynamometer (Biodex ^b, Copyright Biodex Medical Systems, Inc. 2003) at baseline, six months, and at the end of the study (biodex.com). Three reps were performed at each angle and the average peak torque was reported at each angle. The overall average of the values at the three different angles taken at baseline, 6 months, and the end were used for the analysis. Subjects were measures by the same technician (R.M.) on the same machine.
- Informed consent: All participants received a comprehensive explanation of the proposed study, its benefits, inherent risks and expected commitments with regard to time. Following the explanation of the proposed study, all patients were allowed a period of questioning. Individuals who were willing to participate in the study were required to read and sign the informed consent document during the first visit and prior to any experiments (Appendix 9)

Operationalization: The exercise group performed the abdominal and lower back strengthening exercises for 40 minutes, three times a week, over a period of 12 months minimum. The exercises were implemented while lying on the floor in a prone or supine

position (strength calisthenic exercises) or while standing and leaning against a chair for support (weight bearing). Participants started their exercises with a five minutes warm-up. Stretching was included in some of the exercises and at the end of the session. Women in the exercise group were given a descriptive list of the core/lower back strengthening exercises (Appendix 10). Participants in both groups were asked to maintain their regular physical activity assessed at baseline.

Exercise description: A thorough warm-up preparing the back for the exercises to come is completed at first. The muscles that support the spine vary from “extensors” (back and gluteal muscles), to “flexors” (abdominal and iliopsoas muscles), to “obliques” or “rotators” (side muscles). Trapezius, rhomboids, latissimus dorsi (LD), and erector spinae (ES) are the muscles that form the back. Rectus abdominis (RA) and internal/external obliques (O) form the abdomen muscles (www.spine-health.com). This pilot study focused on the LD and ES of the lower back, and on the RA and O of the abdomen. The Rating of Perceived Exertion (RPE) scales were used as a guideline in setting the exercise intensity. Participants were asked to start at a low intensity level (RPE 10-11). A regimen was tailored according to each participant’s fitness level. Subjects were recording the number of sets and reps for each movement at the end of each session. Participants were instructed to gradually go up to a moderate level (RPE 12-13) without exceeding the intensity level of 15 till the end of the study

To strengthen the back muscles, 30-40 minutes of the following core/lower back exercises were done 3 times per week (Appendix 10):

Abdominal Exercise

1-Pelvic lift: Lie on the floor supine position with knees bent, feet shoulder-width apart, and arms to the side; tighten the abdominal muscles, lift the pelvis slightly off the ground

without bouncing, and without using buttocks or leg muscles; hold for 5 seconds, exhale, and slowly release the pelvis back down on the floor while inhaling. After 3 months of exercising, perform the same movement on the Thera-Band Exercise Balls[®], where you put your feet/heels on the ball instead of the floor. Do 2 sets of 15

2-Core strengthening: Lie on the floor supine position with knees bent, feet shoulder-width apart. Grab both knees and press them against the chest. Extend one leg out while exhaling and take it slowly down towards the floor, without letting it touch the floor. The leg should stop from going down at the level when then lower back starts to arch. Once at that level, take your leg back in and repeat with the other leg. Do 2 sets of 10.

3- Standing knee lifts: Stand with right hand holding on to side of chair; raise left knee slowly to 90 degree angle; grab behind left knee with left hand and slowly bring the knee up to the chest; hold it for 5 seconds, keeping the core inwards and exhaling, then lower slowly to the starting position, inhaling. Repeat the same with the other leg. Do 2 times 15 for each leg.

4-Standing leg adduction: Stand with right hand holding on to side of chair. Raise one straight leg slowly to the side keeping the core contracted inwards; exhale, then lower slowly to the starting position, inhaling. Repeat the same with the other leg. Do 2 times 15 for each leg.

PS: Exercises 3 and 4 can be combined together in one exercise where the leg goes from forward bent 90 degrees position to side extended position.

5-Arm/Leg raises: Get down on your hands and knees and keep your core inwards and back in a neutral straight position (cat position); keeping your neck and back straight; slowly lift your right arm and the left leg to make one straight line parallel to the floor along with the back. Your head should be looking towards the floor keeping the neck in a neutral position. Exhale as

you reach out and keep the core inwards. Slowly go back to starting position while inhaling, and repeat the same routine with the other arm and its opposite leg. Do 4 sets of 10

Back Exercises collated from (Hyde, 2001) with some modifications done by the investigator (R.M.).

1-Prone arm/leg exercises: Lie on stomach –prone position, face-down keeping neck straight with legs straight and arms straight overhead; Slowly lift the right arm along with the left leg, exhale, hold for 2 seconds and come down. Repeat with left arm and right leg. Do 4 sets of 10. If the participant fails to accomplish this exercise, he/she can start gradually with lifting each arm alone at first, then each leg, then combining both leg and arm.

2-Back extension: Keep the previous position. Repeat lifting the torso slowly off the ground while keeping the legs on the floor and exhaling, with both arms behind the head and return to start position (10 times). For a harder exercise, repeat stretching the arms out like a cross (10 times), and then stretching the arms forward (10 times). The last advanced exercise can be given in one month from the day of the study.

3- Cat curls: Get down on your hands and knees and keep your core inwards and back in a neutral straight position. Your head should be facing the floor. Curve your back inwards making a C shape towards the floor; rise your head looking upwards while inhaling; hold for 3 seconds; then curve your back outwards in a mountain shape while exhaling; your head should be looking downwards; hold for 3 seconds; go back to neutral position. Do 2 sets of 10.

4-Back stretches: Lie in prone position, lifting the torso up leaning on the elbows. Hold for 10 seconds. Move backward on the bent knees, stretching the arms forward, pulling head between arms. Let your gluteus touch your heels. Hold for 10 seconds. Gently stand on the feet while keeping the torso down; cross the arms and grab behind the knees with the palms. Very

gently arch the back upwards to the ceiling (C shape in the back), while grabbing behind the knees with the palms. Hold for 10 seconds. Gently roll the back all the way up. Repeat the final stretch exercise 5 times.

5.2.1. Statistical Methods

Bone density was taken at baseline (BD_0) and at the end of the study (BD_1). The change in bone density between time 0 and time at the end of the study was calculated for all subjects ($BD_1 - BD_0 = \Delta BD$). Two-way ANOVA was used to test for the differences in change in BMD between the two groups, while blocking for fosamax intake and taking baseline BMD as a covariable. A paired TTEST was used to test the mean difference of BMI, lumbar strength, and lumbar BMD obtained for each group at baseline. Muscle strength was measured at baseline, at the mid, and at the end of the study. Repeated measures analysis was used to test the changes in isometric lumbar strength over time. Repeated measures analysis was also used to test the changes in BMI values between the two groups over time. The Least Significant Change (LSC) was calculated for the GE lunar prodigy DXA scan used at Ochsner. Power analysis using non central t-distribution was used to estimate the sample size needed for the study to observe significant changes in BMD. All statistical computation was implemented using SAS (version 9).

5.2.2. Assumptions

The following pilot study need to be assessed with the following assumptions in mind:

- Women participating in this study were assumed to accurately report their behavior concerning physical activity and dietary intake.
- Women were expected to adhere to the prescribed exercise plan for the entire period of the study, with no loss-to-follow-up.

-Lumbar mineral density and back extensor muscle strength were measured on the same machines (DXA and Biodex, respectively) tested for their validity and reliability.

5.3. Results

Table 5.1 displays the major similarities and differences among the postmenopausal women enrolled in the two groups. All the participants were under 75 years of age based on the inclusion criteria. The three women in the exercise group completed the Back-Core strengthening exercises; surprisingly, all of them stopped their previous physical activity such as walking, bike riding, and weights, and they dedicated their exercise routine to the study exercises. As for the control group, one woman remained inactive, while 3 others kept their previous physical activity (gardening, weights, walking), and another 2 women became more physically active once they were enrolled in the study, where one woman started walking and another woman added swimming, gardening, and weights onto her aerobics routine. The study lasted for about 12 to 13 months. One woman in the exercise group started taking fosamax, after having been enrolled in the study and 4 women in the control group were on fosamax shortly before or during the study. All women were consuming levels of calcium adequate to support bone formation through supplements (8 women) or through diet (1 woman). There was no significant differences between the EG and the CG for any of the baseline variables (strength, BMI, and lumbar BMD). No statistical difference was shown in the BMI change between the 2 groups (Fig. 5.1). However, significant differences were shown in the mean changes in mean lumbar strength (Fig. 5.2) and BMD (Fig. 5.4) in both groups.

At baseline, the BMI values of the 2 groups were not significantly different (TTEST=-0.98; P=0.36); Repeated measures analysis of the BMI changes over time (Table 5.2) showed no significant interaction between group and time (P=0.98) suggesting no significant departure from

parallelism between BMI and time. The between subject variation (group) was not significant either ($P=0.36$) suggesting that BMI values are not far from being coincident between the 2 groups. Similarly, the within subject variation (time) was not significant ($P=0.12$) suggesting no time effect on the BMI.

Table 5.1: Demographics, baseline data, and value changes for exercise and control groups

	Exercise group (n=3)	Control Group (n=6)
Race	3/3 Caucasian	6/6 Caucasian
Exercise Type	3/3 Back-Core	4/6 Walking-weights 1/6 Yard 1/6 Non active
Fosamax	1/3	4/6
Calcium supplements	3/3	6/6
Baseline BMI \pm SD	23.74 \pm 2.35	26.275 \pm 4.08
Baseline Strength \pm SD	45.507 \pm 32.86	65.156 \pm 35.78
Baseline BMD \pm SD	0.972 \pm 0.028	0.944 \pm 0.029
ΔBMI Kg/m² \pm SD	-0.50 \pm 0.76	-0.51 \pm 0.704
ΔStrength ft-lbs (T₂-T₁) \pm SD	+30.03 \pm 11.67*	+21.75 \pm 8.12*
ΔStrength* ft-lbs (T₃-T₁) \pm SD	+64.11 \pm 14.29*	+38.07 \pm 9.99*
ΔBMD/yr* g/cm² \pm SD	+0.019 \pm 0.012	-0.029 \pm 0.051

* $P<0.05$; Δ implies change; (T₃-T₁) implies (final – baseline); (T₂-T₁) implies (6months – baseline)

Fig. 5.2 shows that follow-up measurements at 6 months and at 12 months showed significant changes for mean isometric strength in both groups. The baseline mean strength values were not statistically different between the 2 groups (TTEST=-0.79; $P=0.45$). Repeated measures analysis of mean strength values over time (Table 5.3) showed no significant interaction between the two ($P=0.36$) suggesting no significant departure from parallelism between mean strength and time. The baseline value of strength did not affect the change in response ($P=0.72$). The between subject variation (group) was not significant either ($P=0.24$) suggesting that mean strength values are not far from being coincident between the 2 groups. However, the within subject variation (time) was significant ($P=0.03$) suggesting an increasing trend of the strength values from baseline over time in both groups, as shown in Fig5.3. At

baseline, the average strength for both groups was depicted in Fig5.3 because there was no significant difference between the two values at baseline.

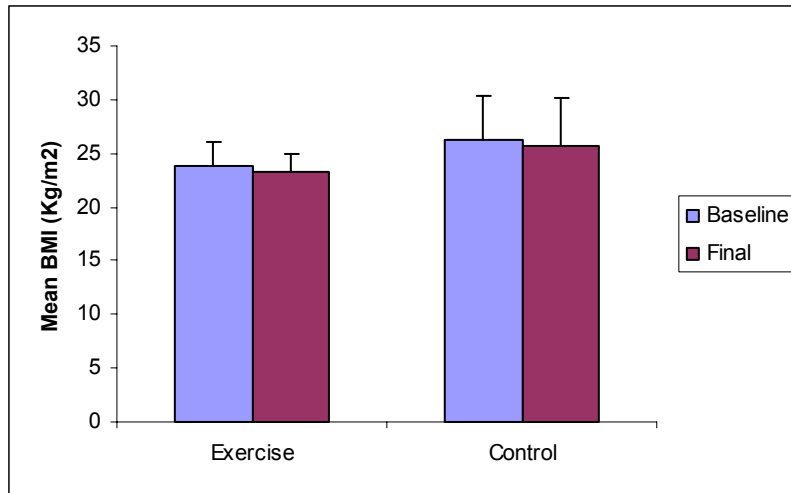


Fig. 5.1: Pre- and Post-training Mean Body Mass Index (BMI) values of exercise (n=3) and control group (n=6)

Table 5.2: Type 3 of fixed effects of BMI values over time in exercise and control groups

Effect	F	P
Group	0.93	0.36
Time	3.08	0.12
Group*Time	0.00	0.98

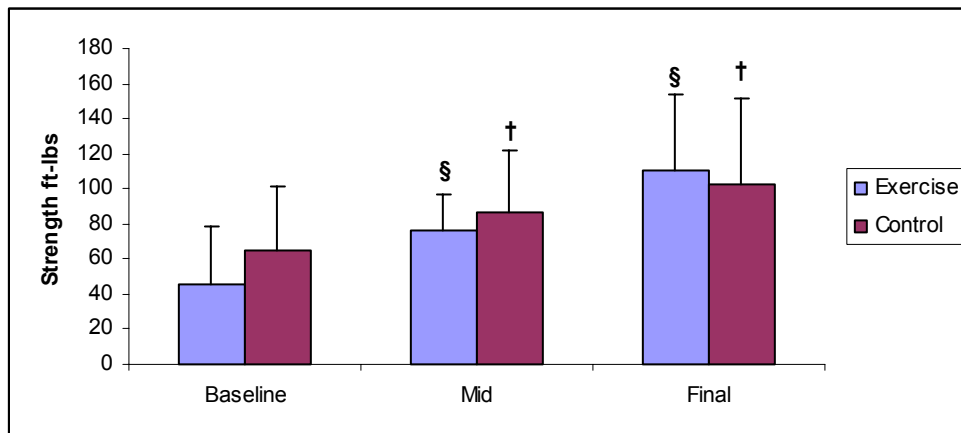


Fig. 5.2: Mean isometric strength values of exercise (E) (n=3) and control group (C) (n=6) at baseline, mid, and end of the study; § P<0.05 in E group vs. Baseline; † P<0.05 in C group vs. Baseline

Baseline lumbar BMD were not significantly different between the 2 groups (TTEST=0.93; P=0.38). The training program resulted in a 0.019 ± 0.012 increase in BMD in the lumbar spine in the exercise group (TTEST=2.70; P=0.05; Fig. 5.4). The 0.029 ± 0.051 decrease in BMD in the lumbar spine in the control group was not statistically significant (TTEST=-1.39; P=0.11; Fig. 5.4). A two-way ANOVA with exercise and fosamax being as the 2 treatments, as well as baseline BMD taken as a covariable, was used to test the difference in BMD change between the two groups. Table 5.4 shows that the one-tailed P value testing the difference between the two groups was not statistically significant (T value=0.9; P=0.21). Table 5.5 shows the steps to calculate the least significant change (LSC) for the DXA machine used. A change in BMD is significant if it exceeds the LSC. In our study, the observed changes in both groups were at borderline of significance and were not too far off the LSC. This prompts the power calculation using non-central t-distribution as shown in Table 5.6 in order to estimate the sample size needed. Given the observed variance of 0.002 and the observed difference ranging from 0.014 to 0.02, the number of subjects per group was generated in order to obtain a power of 0.8. Table 5.7 shows a descriptive comparison of the questionnaires filled at the beginning and at the end of the study by both groups.

Table 5.3: Type 3 of fixed effects of mean lumbar strength values over time in E and C

Effect	F	P
Baseline Strength	0.13	0.72
Group	1.67	0.24
Time	7.39	0.02*
Group*Time	0.92	0.36

* P<0.05;

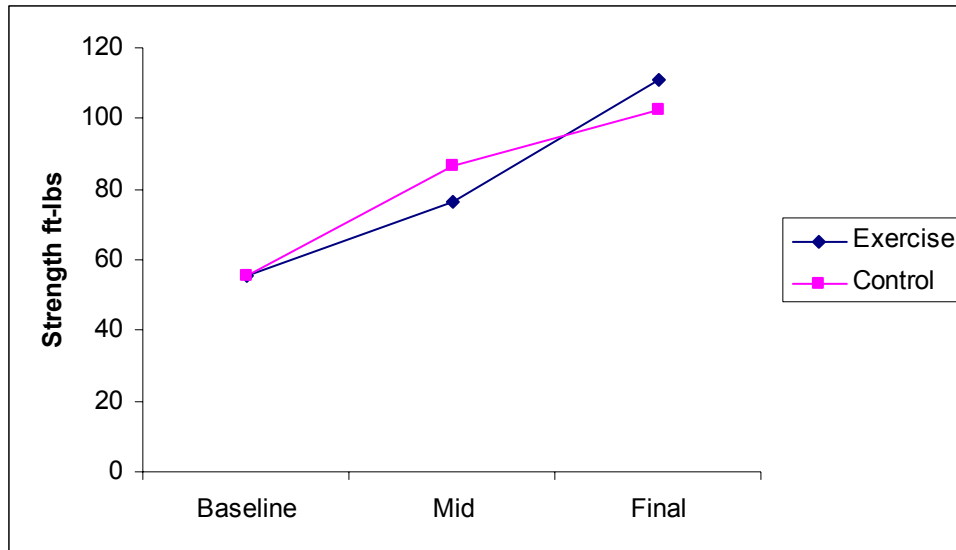


Fig. 5.3: Graphical profile Analysis of mean isometric strength values with time in E (n=3) vs. C (n=6) groups.

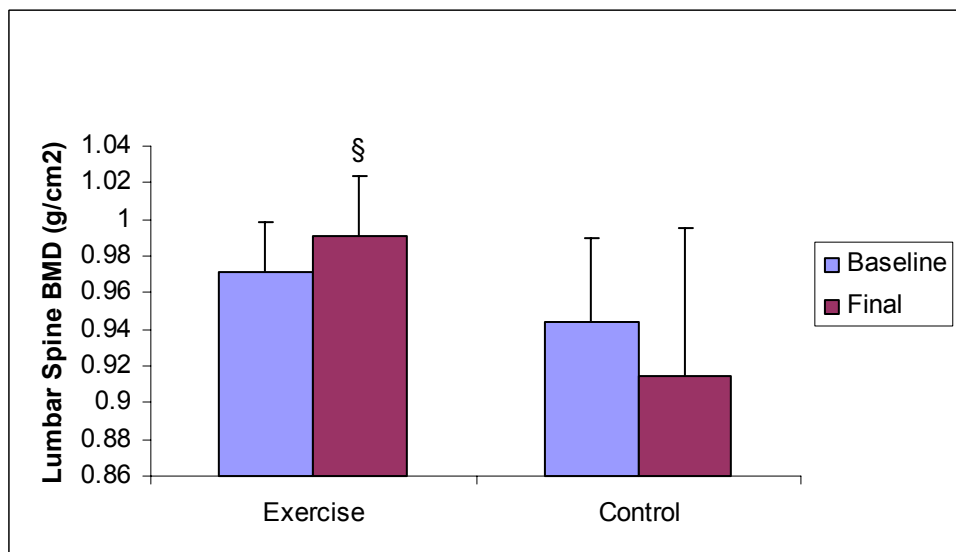


Fig. 5.4: Bone mineral density (BMD) values in lumbar spine in E (n=3) and C (n=6); Values are mean \pm SE; § significantly different from baseline (P=0.05) for paired T-Test

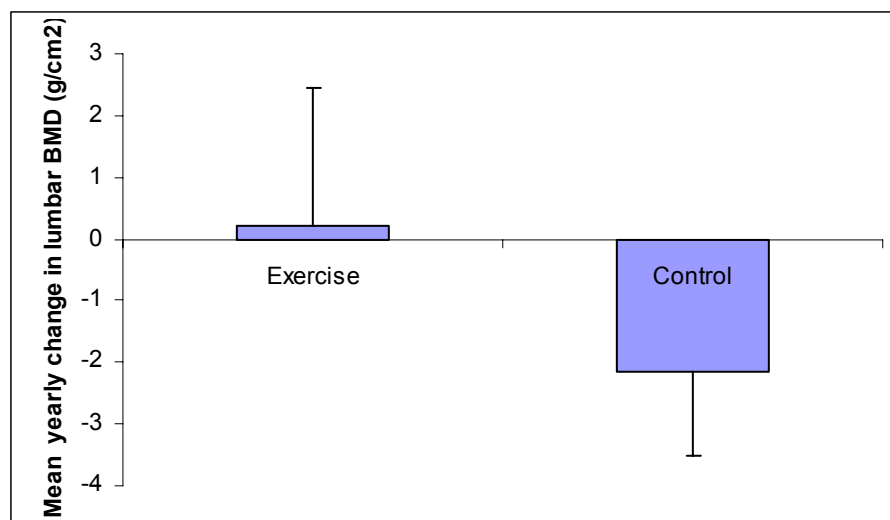


Fig. 5.5: Mean yearly change in BMD in lumbar spine in E (n=3) and C (n=6); Values are mean \pm SE;

Table 5.4: Hypothesis testing results of the mean yearly change in BMD between the E and C groups by 2-way ANOVA with baseline BMD as a covariable

TWO WAY ANOVA			
	Estimate \pm SE	T value	P (1 tailed)
Exercise	0.206 \pm 2.233	0.09	0.46
Control	-2.166 \pm 1.342	-1.61	0.09
Difference	2.373 \pm 2.625	0.9	0.21

Table 5.5: Calculation of the Least Significant Change (LSC) of the DXA machine

Standard Error of the machine	0.01
Variance of one scan	0.0001
Variance of two scans	0.0002
SD of two scans	0.014
Z_{α} (1-tailed)	1.645
Margin of Error= Z_{α} * SD= LSC	0.0232

Table 5.6: Sample size calculation for observed variance of 0.002; a power of 0.8; and an observed difference varying from 0.02 to 0.039

diff	n	power
0.020	80	0.80268
0.020	82	0.81235
0.021	74	0.80990
0.022	66	0.80096
0.022	68	0.81270
0.023	62	0.81082
0.024	56	0.80369
0.024	58	0.81742
0.025	52	0.80608
0.026	48	0.80483
0.027	46	0.81712
0.028	42	0.80933
0.029	40	0.81704
0.030	36	0.80146
0.031	34	0.80408
0.032	32	0.80445
0.033	30	0.80242
0.036	26	0.81227
0.037	24	0.80115
0.039	22	0.80666

$$\text{Power} = \Pr. (t \geq t_{\alpha/2, \gamma}) \\ = 1 - F(t_{\alpha/2, \gamma}; c; \delta)$$

γ = degrees of freedom

$$\delta = \text{non central parameter} = \frac{\mu_1 - \mu_2}{\sigma \sqrt{\frac{2}{n}}}$$

Table 5.7: Comprehensive pre- and post-comparison of the questionnaires for E and C groups

Questionnaires	Exercise group	Control group
Pre-Post comparisons		
Health Status	1/3 no change	5/6 no change
Questionnaire	2/3 Improvement*	1/6 persistent low back pain
Short Form-36	3/3 Improvement†	5/6 no change
		1/6 Deterioration‡
FFQ§	3/3 no change	6/6 no change

*Less low back pain; better performance; better health related attitudes; † Less feelings of tiredness; greater health expectations; increased feelings of wellness, calmness, and peacefulness; ‡ Health limitations to do the work and social activities; pain interfering with work; bone fracture in a fall; §FFQ = Food Frequency Questionnaire.

5.4. Discussion

The ideal situation was that the design would be pair matched where each pair of women would be matched for the different variables such as medication, physical activity, baseline lumbar BMD, and baseline lumbar isometric strength. A paired TTEST would have taken care of the analysis nicely. However, the actual situation was different, where it was hard to recruit the women into a 1-year exercise study. Thus, the experimental design alone was not able to control for the differences among the participants, albeit these variations between the individuals were controlled with the statistical analysis to some degree. A two-way ANOVA with baseline BMD taken as a covariable was run to control for the interaction of fosamax with the exercise.

All women in the study were asked to take 1000-1500 mg of calcium supplements because it has been suggested that exercise alone would not maintain or increase the bone mineral density if there were no calcium available from the diet or supplements. In fact, in a critical review of the literature, Specker (1996) found indirect evidence that the beneficial effects of exercise on bone density may only happen if the daily calcium intakes exceeded 1000 mg/day. In a similar fashion, Wymelenberg (1994) recommended in the Harvard Health Letter that a woman needed to increase her daily calcium intake to 1500 mg when she approached menopause because this is when estrogen production starts to attenuate, thus resulting in a decrease in calcium absorption. Likewise, McGarry et al (2003) have suggested that postmenopausal women should be taking the upper end of the range (1200-1500 mg).

Although the women were asked to maintain their baseline physical activity during the whole study, unfortunately, the opposite effect happened; women in the E group dedicated their commitment to the study exercises and stopped their previous habitual routine; conversely, 2 of

the women in the C group became more active once enrolled in the study. This interviewer bias confounded the results.

According to Sinaki and Mikkelsen, (1984), they concluded from their controlled trial on postmenopausal women that flexion exercises were causing an increased number of vertebral fractures; whereas extension exercises as well as abdominal strengthening exercises were important to increase lumbar BMD. The author Meeks (1999) also discourages the performance of flexion exercises (such as abdominal sit-ups) in postmenopausal women. Based on these findings, our exercises were designed as such, with the exclusion of the sit-ups for the abdominal work-out.

According to Steinschneider et al., (2003), when women lose weight, the bone area might appear larger on the DXA scan due to the loss of muscle and fat tissue, leading to an artifact of a decrease in BMD. Luckily, this pilot study showed that the numerical decrease in BMI in both groups was non significant with time, where the BMI remained constant in both groups (Table 5.2).

Some studies have shown positive effects of different training regimens on muscle strength. Rhodes et al. (2000) have shown that a one-year progressive resistance exercise increases dynamic muscular strength in healthy sedentary postmenopausal women ($P < 0.01$). Similarly, Morganti et al. (1995) have reported a similar increase in strength in elderly women who performed a series of strength exercises using machines over a period of one year. The findings of these studies were consistent with the present study; however, the exercises given here were strength exercises with no weights. Mean isometric lumbar strength appeared to significantly increase from baseline in both groups. One explanation as to why the control group increased in lumbar strength might be their engagement into physical activity after having been

enrolled in the study. In fact, their willingness to participate in the study is a reflection of their interest in the exercise training. Note that the baseline isometric strength value of the control group was numerically higher than the exercise group. Yet, it became numerically lower than the exercise group at the end of the study. These results suggest that the core/lower back strengthening exercises did increase isometric muscular strength in post-menopausal women with osteopenia in the lower back.

Our findings also suggested a borderline numerical but non-significant difference between the 2 groups (2.373 ± 2.625) in lumbar mineral density ($P=0.21$). In a recent meta-analysis in 2000, Wallace and Cumming found in their literature search conducted between 1977 and 1998 that non-impact exercises (strength training with weights) had a positive effect on the lumbar mineral density (around 1%) in pre-and postmenopausal women. Yet, there their search was limited to randomized controlled trials. On the other hand, our pilot study did not include weights. Another study that did not include weights done by Beverly et al (1989) showed that grip strength and BMC increased in the forearm of the exercising older women after having squeezed on a tennis ball as hard as possible for 30 seconds each day for 6 weeks. This suggests that short period of a site-specific skeletal stress may induce osteogenesis.

According to Drinkwater (1994), and congruent with the findings in the case referent study in chapter III, the bone that has the lower BMD at baseline would show a greater response or increase to treatment compared to bone with a higher BMD. Similarly, this principle applies to the type of bone where trabecular bone is more responsive to treatment than cortical bone. This can also apply to individuals, as Drinkwater (1994) had mentioned. In our study, the women in the exercise group had a numerically higher lumbar BMD at baseline, as compared to the C group (fig.5.4). Yet, the exercises still showed a numerical but not significant increase in

the lumbar mineral density in the E group as compared to the C group.

Another meta-analysis of randomized and non-randomized clinical trials conducted by Wolff et al (1999) suggested that there was a preventive effect or a reversed bone loss by almost 1% per year caused by the exercise training, regardless of menopausal status of the women. Furthermore, Wolff's findings suggested that the overall effect of the non-randomized clinical trials was almost double of those randomized suggesting a positive confounding bias due to the non-randomization. To minimize this bias in our study, we controlled for different variables in the statistical analysis by including them in the model. The diversity of the type, intensity, duration, and frequency of the exercises used made the development of specific recommendations for exercises for these women almost impossible. In our study however, our exercises consisted of site-specific strengthening exercises for the core and lower back, and they were performed by postmenopausal women with osteopenia in the lower back at a low-to moderate intensity 3 times per week, 40 minutes each time. Nevertheless, these home-based core/lower back strengthening exercises should serve as a complement to, rather than a surrogate for, the woman's aerobic exercise routine.

There is a paucity of exercise studies done in early postmenopausal women, as recently discussed in a review article by Wallace and Cumming (2000). Literature regarding the type of strengthening of exercises used in our pilot study per se is limited in early postmenopausal women. Sinaki et al. conducted the closest exercise regimen to ours in 1989, where a total of 65 healthy postmenopausal women (age 49-65 years) were randomly allocated to either an exercise group or a control group. The exercise group was engaged in back strengthening exercises, for a frequency of once a day, 5 times a week, for 2 years. All the women were not on calcium/vitamin D supplements. The results showed no significant differences in the rate of

vertebral bone losses between the 2 groups. Both groups increased in muscle strength but it was more significant in the exercise group. Although the results in Sinaki et al's study were not very different from our results, there are some inherent differences in the designs followed; first, the women enrolled in our study had osteopenia as opposed to the healthy women in Sinaki et al's study; second, all of our subjects were on calcium supplements as opposed to Sinaki et al's study where only 50% of the participants of both groups had an adequate dietary calcium intake in the range of 1200 mg. It has already been discussed that a healthy bone would show less improvement than a sick bone, and that calcium supplements are the hallmark of exercise-induced gains in bone mineral content. On the other hand, in a study conducted on rats, Hsieh and Turner (2001) have found that "increasing load frequency" of an exercise is one way to promote osteogenesis. On the other hand, Drinkwater (1994) talked about the "specific exercise overload" to the skeletal system that would create an osteogenic response in the elderly, had the exercise been indeed an overload. Likewise, the literature suggests that in order for an exercise to meet the osteogenic criteria, the exercises should include a high-magnitude load bearing activities with few repetitions (Skerry, 1997). However, this principle might be harmful to elderly people who may not tolerate such a strenuous exercise. The advantage of our study is that the exercises implemented are safe, with low-magnitude overload, and more frequency.

Our proposed hypothesis to explain the expected increases in regional BMD with the core/lower back strengthening exercises is that the site-specific lower exercises cause the muscle to pull on the bone. The importance of site-specificity of the exercises to increase the BMD in the targeted area has been mentioned by a plethora of researchers (Beck and Snow, 2003; Kerr et al., 2001; Kerr et al., 1996). The exercises in our pilot study target opposite muscle groups (the abdominals and the lower back). Thus, the same muscle is contracted when it is activated by the

exercise, and then it is stretched when the opposite muscle group is activated. This versatile pulling action of the muscle in opposite directions for many sets and repetitions creates strains on the bone, which are then translated into biochemical signals, as suggested by Lanyon and Hartman (1977) that might induce bone cell activity, leading to osteogenesis at the points of the pulling action. According to Lane et al., (2003), the combination of muscle pull and direct impact initiate bone loading. Additionally, findings revealed that performing the exercises for 3-5 repetitions may create enough overload to activate the dormant muscle fibers and thus improve muscle strength in frail individuals (Hyatt, 1996). In fact, Frost (1997) explained in his article about the “modeling threshold” principle of the bone; that is the muscle forces should induce strains on the bones that exceed its modeling threshold, which will lead to an increase in bone mass and bone strength.

The non-statistical significance seen in this study may be due to the small sample size. Given the variance estimate of the population, the expected difference, and the power, a sample size of 80 people per group is needed for an observed difference of 0.02 and a sample size of 22 per group is needed for an observed difference of 0.039.

On another note, it has been suggested that it is unfair to judge on the effectiveness of these exercises by regarding the BMD increase as the sole monitoring tool. Recent emerging evidence highlights that there has been no studies that show a positive correlation between BMD increments and patient outcomes (Crandall, 2001); additionally, the regression to the mean phenomenon may lead to a biased result (Cummings et al., 2000); finally, some studies have suggested that the reduction of fractures owing to the exercise treatment is a better reflection of the exercise benefit than the BMD increments (Cummings et al., 2002).

According to Tomporowski (2003), physical activity is associated with psychological well-being. It has been recognized in the literature that exercise promotes good health and longevity. Similarly, in our pilot study, the women in the exercise group showed increased feelings of wellness, calmness, and peacefulness at the end of the 1-year exercise period based on the SF-36 questionnaire that they filled out pre- and post- the exercise study period. They also reported less feelings of low back pain. On the contrary, the control group either showed no change in their feelings of wellness, or even worsening. One woman in the control group fractured a bone in a fall. This suggests that the core/lower back exercises may also be beneficial to maintain balance and stability and this may help preventing the women from falls. According to Rutherford (1999), a myriad of variables lead to the increase or a decrease of a fracture risk. Factors such as low bone density, increased age, muscle weakness, and poor balance might accentuate the risk of falling, and thus increase the risk of fracture. Thus, as Shephard mentioned in 2002, the importance of physical activity in elderly is not only to increase bone density per se, but also to reduce the risk of falls. Thus, it is wise to design exercises to the elderly population that tend to increase muscle strength as well as improve balance in order to control for the risk of falls and thus reduce the risk for fractures. The site-specific core/lower back strengthening exercises were specifically designed for this purpose. Our pilot study suggests that these site-specific exercises increase lumbar strength, and may potentially improve lumbar mineral density. This may lead to a better body balance and a decreased risk of fall.

5.4.1. Limitations

The prescribed exercise program in the current study did not completely comply with the ACSM exercise recommendations which states that an exercise session should comprise a warm-up period (approximately 10 minutes), an endurance phase (20 to 60 minutes), an optional

recreational game, and a cool-down period (5 to 10 minutes) (ACSM, 2000). In the present study, however, the primary objective was to focus on some site-specific calisthenics exercises for the lower back and study their effect on the lumbar bone mineral density and strength. A warm-up and a stretching were always given at the beginning and at the end of each session respectively.

A second limitation is that the proposed study was a pilot study limited to Ochsner patients in Baton Rouge; Due to this sampling bias, the results cannot be generalized to the entire population of women with low bone density. Results should be interpreted with caution. Moreover, subjects provided self-reported information regarding exercise and diet, including the prescribed exercise they did at their home if they missed one session. The accuracy of this information is subject to bias.

A third limitation was that neither the sampling nor the allocation of treatment was random. Due to the difficulty in recruiting women to be part of the exercise study, only those who showed interest in being involved in the study were selected. This accentuated the selection bias and might have affected the results.

A fourth limitation was the small sample size for this pilot study. Again, this delineates the difficulty in implementing a 1-year longitudinal exercise study.

A fifth limitation was that some of the bone scans that were assessed at baseline might have been taken 3 months prior to the start of the study. The change in BMD that might have occurred in these 3 months was considered negligible.

A sixth limitation was that one woman in the exercise group did not report consuming adequate amount of calcium and thus had to be excluded from the analysis.

5.5. Conclusion

The site-specific core/lower back strengthening exercises implemented at a low to moderate intensity, 3 times per week, 40 minutes each time, appear to significantly improve isometric lumbar strength (when complemented with calcium supplements), enhance the feelings of wellness. They may potentially increase lumbar mineral density and may reduce the likelihood of back pain.

5.6. Recommendations

The site-specific core/lower back exercise should be part of a woman's weekly routine of physical activity since these muscles are neglected in one's typical daily activities. These exercises may improve trunk muscle strength and stability, which may reduce the risk of falls and increase comfort and spine BMD. Because of the limited sample size, it is highly recommended that more studies need to target the design of specific exercises that can be safe, osteogenic, and practical to the postmenopausal women who may not be able to engage in weight loading activities owing to the low bone mass.

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Suppliers:

- a. Biodex; System 3; Model number: 835-000; Dual position back extension/flexion attachment's model number: 830-450. Biodex Medical Systems Incorporation; 20 Ramsay Road; Shirley, New York 11967-4704, USA; www.biodex.com
- b. DXA: GE Lunar Prodigy; GE Healthcare Lunar Corporation; 726 Heartland Trail, Madison, WI 53717 USA
- c. Theraband; the Hygienic Corporation, 1245 Home Ave, Akron, OH 44310, USA; www.Thera-BandAcademy.com;

CHAPTER VI CONCLUSIONS

Three projects were conducted to approach the problem of osteoporosis/osteopenia in postmenopausal women in Baton Rouge.

The results of the first study (chapter 3) indicated that responding physicians displayed poor knowledge regarding osteoporosis prevention with gonadal steroids in hypogonadal patients; control of caffeine intake because of its calciuretic effect; osteoporosis diagnosis with X-rays; DXA scan recommendation upon glucocorticoid use; DXA scan recommendation for all women above 65 years of age; and the appropriate kind of exercise for osteoporosis treatment. Rheumatologists and endocrinologists scored globally better on osteoporosis management. Physicians with more years of experience were more knowledgeable of osteoporosis care.

The results of the second study (chapter 4) indicated that osteoporosis management lied partly on patient adherence. Barriers to adherence varied from physiological reactions to a specified treatment to a lack of motivation from the patient. Moreover, the change in BMD under a specific treatment could vary from a decrease, to maintenance, or to an increase in BMD, without necessarily achieving the normal BMD range. Spine, the area mostly affected, showed more improvement with treatment than the femur. Bisphosphonates acted best on the spine statistically and on the femur numerically. An anti-resorptive treatment may be needed if the disease was advanced. Ultimately, low BMI, genetics, and history of fractures were negatively correlated to the increase in BMD. Thus, these risk factors for osteoporosis are also risk factors for further progression of the disease as seen by decreased BMD in this study.

The results of the third study (chapter 5) suggested that site-specific core/lower back strengthening exercises could significantly improve isometric lumbar strength (when complemented with calcium supplements), potentially increase lumbar mineral density, enhance

the feelings of wellness, and may reduce the likelihood of back pain in postmenopausal women with osteopenia. These exercises were implemented at a low to moderate intensity, three times per week, 40 minutes each time.

Ultimately, for a better management of osteoporosis, physicians need to expand their knowledge in this arena and to be more involved in motivating their patients to improve patient compliance. Although no specific recommendations for an osteogenic exercise can be developed from our studies, the researchers do agree however that physical activity is preferred over inactivity (Hertel and Trahiotis, 2001).

It is highly recommended that more long-term studies with greater number of subjects are needed to target the design of specific exercises that can be safe, osteogenic, and practical to the postmenopausal women who may not be able to engage in weight loading activities owing to the low bone mass.

6.1. References

Hertel, K. L., & Trahiotis, M. G. (2001). Exercise in the prevention and treatment of osteoporosis: The role of physical therapy and nursing. *Nurs Clin North Am*, 36(3), 441-453, viii-ix.

APPENDIX 1: SURVEY QUESTIONNAIRE

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June 27, 2002

SURVEY FOR OUR BATON ROUGE PHYSICIANS WHO TREAT OSTEOPOROSIS

Dear Dr.,

I am Rania Mekary, a PhD candidate at LSU in the Human Nutrition Division, conducting a survey for a research project on osteoporosis. In advance, I am thanking you for taking the time to fill out this questionnaire, a necessary step towards completing my dissertation.

This survey is a part of an important research being conducted by Louisiana State University's School of Human Ecology concerning osteoporosis. The aim of the survey is to determine the effectiveness of the steps physicians in the Baton Rouge area take to **prevent, diagnose, treat, and follow-up** with their patients who are at risk of - or already suffering from - osteoporosis. Who should have Bone Mineral Density measurements? Who should be treated? What is the best-recommended treatment so far? How efficient is the treatment prescribed? Are there any improvements on serial test in bone density in patients' prescribed treatments? Hopefully, answers to these questions will be derived once the data is gathered and analyzed from this questionnaire. Subsequently, **the results will be made available to you for your information and use**. I hope these results will be helpful to your future treatments of osteoporosis patients, and ultimately to the patients themselves.

While I know your time is very valuable, so is your input for this survey. These questions were designed to be easily answered with the minimal amount of time required. Your collaboration will be highly appreciated and will be very useful to further our education in this endeavor. Should you have any comments or suggestions, please feel free to contact me or e-mail me at the address above.

Very Sincerely,

Rania Mekary

Important: This file is a Word Document. **Please press the <Tab> button or the “up” and “down” arrows, or the mouse to navigate across the questions. Refrain from using the <Enter> button when filling out this form.** If you pressed <Enter> by mistake, click the “Undo” Icon from the toolbar on top of your screen to restore the form to its original format. Thank you.

1. **Today’s Date:** (MM-DD-YYYY)
2. **Doctor’s information:**
 - a. Specialty: ☐ Endocrinologist ☐ Family Practice ☐ Internal Medicine
☐ OBGYN ☐ Orthopedic ☐ Rheumatologist
☐ Other (Please Specify)
 - b. Years of Experience
 - c. Hospital name
3. **Do you have or have you seen patients with osteoporosis?**
 - a. ☐ If no, please stop here and submit the questionnaire as instructed at the bottom of the survey.
 - b. ☐ If yes, approximately how many patients per month?
Please, continue filling out the questionnaire.
4. **What preventive measures do you prescribe before osteoporosis occurs? (Mark all that apply):**
 - a. ☐ Encourage a high calcium diet and exercise to obtain optimal peak bone mass at young age.
 - b. ☐ Prescribe gonadal steroids in men and women who are found to be hypogonadal.
 - c. ☐ Control of alcohol intake and smoking
 - d. ☐ Control caffeine intake
 - e. ☐ Control salt intake
 - f. ☐ Control protein intake
 - g. ☐ Other (please specify)
5. **When do you suspect the presence of osteoporosis? (Please select all that apply):**
 - a. ☐ Pain
 - b. ☐ Loss of height
 - c. ☐ Frailty
 - d. ☐ Curved back
 - e. ☐ Fractures
 - f. ☐ Low peak bone mass at early ages
 - g. ☐ Low body weight (thin individual)
 - h. ☐ Smoking
 - i. ☐ Family history of osteoporosis
 - j. ☐ Other (please specify)

6. What methods do you use to detect osteoporosis before fractures occur?
- ☐ Bone density scan by dual energy x-ray absorptiometry (DEXA)
 - ☐ X-ray
 - ☐ Blood and urine tests for bone markers
 - ☐ Physical examination
 - ☐ Quantitative ultrasound for bone density
 - ☐ History taking
 - ☐ None
 - ☐ Other (please specify)
7. When do you recommend a bone density scan? (Please check the appropriate box):
- ☐ When osteoporosis is suspected, before fractures occur
 - ☐ When see clinical risk factors (premature menopause, amenorrhea, steroid therapy, overactive thyroid gland, bowel disease, anorexia nervosa, family history, poor diet, excessive alcohol consumption, cancer, smoking, etc.)
 - ☐ When fractures have already occurred
 - ☐ To assess the effectiveness of a treatment given for osteoporosis
 - ☐ Upon glucocorticoid use
 - ☐ All post-menopausal women
 - ☐ All post-menopausal women not on hormones
 - ☐ All women above 65 years of age
 - ☐ All men above 65 years of age
 - ☐ Other (please specify)
8. If not insured, what is the % of patients who would do the bone scan anyway? %
9. When do you consider using the bone density scans (DEXA):
- ☐ Always, as a screening tool
 - ☐ Only for women at risk of osteoporosis because DEXA is expensive
 - ☐ Never
 - ☐ Other suggestions (please specify)
10. What treatment do you prescribe for osteoporosis? (Select all that apply):
- ☐ Exercise. If yes,
 - What kind?
 - ☐ Resistance
 - ☐ Swimming
 - ☐ Non weight bearing
 - ☐ Running
 - ☐ Walking
 - ☐ Physical therapy
 - ☐ Other (please specify)

ii. Frequency?

1. ☐ 1 time/week
2. ☐ 2 times/week
3. ☐ 3 times/week
4. ☐ 4 times/week
5. ☐ Other (please specify)

iii. Duration each time?

1. ☐ 10-15 minutes/time
2. ☐ 16-30 minutes/time
3. ☐ 31-45 minutes/time
4. ☐ Other (please specify)

b. ☐ Diet change. If yes, how?

- i. ☐ More dairy products
- ii. ☐ More fortified milk and cereals
- iii. ☐ Other (please specify)

c. ☐ Supplements. If yes, what kind?

- i. ☐ Calcium supplements
- ii. ☐ Vitamin D supplements
- iii. ☐ Other (please specify)

d. ☐ Hormone therapy. If yes, what type?

- i. ☐ Estrogen
- ii. ☐ Progesterone
- iii. ☐ Combination of both
- iv. ☐ Evista
- v. ☐ Testosterone
- vi. ☐ Other (please specify)

e. ☐ Biphosphonates:

- i. ☐ Fosamax
- ii. ☐ Actonel
- iii. ☐ Etidronate

f. ☐ Nasal Calcitonin

g. ☐ Other treatment (s) (please specify)

11. How often do osteoporosis patients come back for follow-up (for another DEXA)?

- a. ☐ Every 6 months
- b. ☐ Every 1 year
- c. ☐ Every 2 years
- d. ☐ Other (please specify)

12. Upon follow-up, what is the approximate percentage of patients in whom you see any improvement in bone density? (0-100%)

- a. Diet and Supplements %
- b. Hormones %
- c. Biphosphonates %
- d. Calcitonin %

13. In case of improvement, how do you describe it? (Give approximate percentage)

- a. Decrease in rate of bone loss %
- b. Net increase in bone mass %
- c. Maintenance of bone density %
- d. Fracture prevention %

14. Do you think the patients follow your prescription?

- a. ☐ Completely
- b. ☐ Partially
- c. ☐ No
- d. ☐ Other (please specify)

15. Which do you think is the best treatment for osteoporosis?

- a. ☐ Supplements / Diet
- b. ☐ Exercise
- c. ☐ Hormone Replacement Therapy
- d. ☐ Biphosphonates
- e. ☐ Calcitonin
- f. ☐ Combination of (please specify e.g. a,c,d, etc.)
- g. ☐ Other (please specify)

16. Osteoporosis patient information:

- a. What age range covers most of your patients in the last year?
Maximum age you have seen: Minimum age you have seen:
- b. What approximate percentages (%) do you characterize your patients to be?
 - i. Sex: % Male % Female
 - ii. Race: % African American % Native American
 %Caucasian % Hispanic

17. When osteoporosis is diagnosed, which areas are most affected in your patients (%)?

% Spine % Hip % Wrist
 % Other areas (please specify)

☐ END OF SURVEY

THANK YOU FOR YOUR COOPERATION.
HOPE YOU HAVE A GREAT DAY!

APPENDIX 2: SUMMARY OF GUIDELINES FOR OSTEOPOROSIS MANAGEMENT BASED ON THE LITERATURE

A. Osteoporosis Prevention

High calcium diet and exercise

Control of alcohol and smoking

Gonadal steroids in men and women if hypogonadal

Control of caffeine intake

Control of salt intake

Others (calcium supplements, exercise, screening, bisphosphonates, PTH assessment)

Control of protein intake

B. Osteoporosis Diagnosis

B.1. Signs of Osteoporosis Presence

Fracture

Loss of height

Curved back

Family history

Smoking

Low Body Weight

Frailty

Low Peak Bone Mass (PBM) at early ages

Pain

Other (steroid use, white race, post-menopausal, amenorrhea)

B.2. Detection Methods Before Fractures Occur

DXA

History taking

Physical examination

Blood and urine tests for bone markers

Quantitative ultrasound for bone density

B.3. Bone Density Scan Recommendation

When osteoporosis is suspected, before fractures occur

When see clinical risk factors (premature menopause...)

To assess effectiveness of a given treatment

When fractures have already occurred

Upon gluco-corticoid use

All women above 65 years of age

C. Osteoporosis Treatment

Treatment

Supplements : 1000-1500mg calcium ; 400-800 IU vitamin D

Exercise: walking ; resistance ; weight-bearing

Bisphosphonates: Alendronate (Fosamax), risedronate (Actonel), and etidronate (Didronel)

Hormone therapy: Estrogen & Progesterone

Selective Estrogen Receptor Modulator: Raloxifene (EVISTA)

Para-Thyroid hormone: Forteo

Diet change: more dairy and fortified milk

Nasal calcitonin

PS: Calcium and vitamin D supplements are a must for every post-menopausal woman even if another treatment is given to treat osteoporosis.

D. Osteoporosis Follow-up

1-2 years if patients are on bisphosphonates

2-4 years if patients are on calcitonin, hormone replacement therapy, or evista.

APPENDIX 3: TELEPHONE SCRIPT

Investigators: Lindsey/ Hegsted/ Mekary	Sites: Ochsner	Protocol: Osteoporosis treatment
Telephone Script		
Subject's Initials:	Subject's #:	Date Performed:

1. Good morning/afternoon/evening Mrs. _____.

“Hello, this is Rania Mekary. I am a PhD candidate at LSU working with Dr Stephen Lindsey on a research study concerning osteoporosis treatment.

You have been randomly selected among 200 patients. I would like to ask you if you don't mind answering a few questions that will shed some light on the study we are doing.

--If the interviewed person gave a verbal agreement, I will document the verbal consent; then I will go ahead and ask the following questions:--

Q1. Are you taking any medication for osteoporosis? If yes, for how long?

Q2. Are you following the physician's prescription (I would read the prescription written by the physician on the medical record)? If yes, skip Q3.

Q3. Why not?

Q4. What is your current level of physical activity? What type of physical activity do you perform? How frequent? How long do you go for?

**Thank you for your time and cooperation.
Have a great day!”**

After the phone call, complete the form, sign and file in the participants' study folder.

Investigator's signature: _____ Date: _____

APPENDIX 4: PHYSICAL ACTIVITY READINESS QUESTIONNAIRE

Subject's Name:		Subject's Code:	
Physical Activity Readiness Questionnaire (PAR-Q)			
Investigators: Lindsey/ Wood/ Hegsted/ Mekary	Ochsner-LSU	Time Performed:	Date Performed:

YES NO

- _____ 1. Has your doctor ever said that you have a heart condition and that you should only do physical activity recommended by a doctor?
- _____ 2. Do you feel pain in your chest when you do physical activity?
- _____ 3. In the past month, have you had chest pain when you were not doing physical activity?
- _____ 4. Do you lose your balance because of dizziness or do you ever lose consciousness?
- _____ 5. Do you have a bone or joint problem that could be made worse by a change in your physical activity?
- _____ 6. Is your doctor currently prescribing drugs (for example, water pills) for your blood pressure or heart condition?
- _____ 7. Do you know of any other reason why you should not do physical activity?

NOTE: 1. This questionnaire applies only to those 15 to 69 years of age.

2. If you have temporary illness, such as a fever or cold, or are not feeling well at this time, you may wish to postpone the proposed activity.
3. If you are pregnant, you are advised to discuss the "PARmed-X for Pregnancy" form with your physician before exercising.
4. If your health changes so that you then answer YES to any of the above questions, tell your fitness or health professional. Ask whether you should change your physical activity plan.

I have read, understood and completed this questionnaire.

SIGNATURE _____ DATE _____

SIGNATURE OF PARENT _____
OR GUARDIAN (for participants under the age of majority)

Witness _____ Date _____

Informed use of the PAR-Q: The Canadian Society for Exercise Physiology, Health Canada, and their agents assume no liability for persons who undertake physical activity, and if in doubt after completing this questionnaire, consult your doctor prior to physical activity.

APPENDIX 5: PHYSICAL ACTIVITY QUESTIONNAIRE

Subject's Name:		Subject's Code:	
Physical Activity Questionnaire			
Investigators: Lindsey/ Wood/ Hegsted/ Mekary	Ochsner-LSU	Time Performed:	Date Performed:

This survey is conducted to assess lifestyle factors related to health.

- Most individuals find that the questionnaire can be completed in approximately 20-30 minutes.
- Replies are important from all participants; exercisers or non-exercisers.
- Be as accurate as possible, but provide your best estimate if you do not remember precisely.
- Please provide information pertain to the previous **month**.

If you wish to comment on any of the questions or to qualify your answers, please write in the margins. Your comments are welcome and will be taken into account.

THANK YOU FOR YOUR HELP!

In this section we would like to ask you about your current physical activity and exercise habits that you perform regularly, at least once a week. Please answer as accurately as possible. Circle your answer **or** supply a specific number when asked.

EXERCISE/PHYSICAL ACTIVITY

- For the last **one month**, which of the following moderate **or** vigorous activities have you performed **regularly**? (*Please circle **YES** for all that apply and **NO** if you do not perform the activity, provide an estimate of the amount of activity for all marked **YES**. Be as complete as possible.*)

Walking

NO YES → How **many** sessions per week? _____
 How many miles (or fractions) per session? _____
 Average duration per session? _____ (minutes)

What is your usual pace of walking? (*Please circle one*)

CASUAL or
STROLLING
(< 2 mph)

AVERAGE or
NORMAL
(2 to 3 mph)

FAIRLY or
BRISK
(3 to 4 mph)

BRISK
STRIDING
(4mph or faster)

or

Stair Climbing

NO YES → How many flights of stairs do you climb **UP** each **day**? _____
 (1 flight = 10 steps)

Jogging or Running

NO YES → How many sessions per week? _____
 How **many** miles (or fractions) per session? _____
 Average duration per session? _____ (minutes)

Treadmill

NO YES → How many sessions per week? _____
 Average duration per session? _____ (minutes) Speed?
 ____ (mph) Grade? ____ (%)

Bicycling

NO YES → How many sessions per week? _____
 How many miles per session? _____
 Average duration per session? _____ (minutes)

Swimming laps

NO YES → How many sessions per week? _____
 How many miles per session?
 (880 yds = 0.5 miles) _____
 Average duration per session? _____ (minutes)

Aerobic Dance/Calisthenics/Floor Exercise

NO YES → How many sessions per week? _____
Average duration per session? _____ (minutes)

Moderate Sports

**(e.g. Leisure volleyball, golf (not riding),
social dancing, doubles tennis)**

NO YES → How many sessions per week? _____
Average duration per session? _____ (minutes)

Vigorous Racquet Sports

(e.g. Racquetball, singles tennis)

NO YES → How many sessions per week? _____
Average duration per session? _____ (minutes)

Other Vigorous Sports

or Exercise Involving

Running (e.g. Basketball, soccer)

NO YES → Please specify _____
How many sessions per week? _____
Average duration per session? _____ (minutes)

Other Activities

NO YES → Please specify _____
How many sessions per week? _____
Average duration per session? _____ (minutes)

Weight Training

(Machines, free weights)

NO YES → How many sessions per week? _____
Average duration per session? _____ (minutes)

**Household Activities (Sweeping, vacuuming,
washing clothes, scrubbing floors)**

NO YES → How many hours per week? _____

Lawn Work and Gardening

NO YES → How many hours per week? _____

2. How many times a week do you engage in vigorous physical activity long enough to work up a sweat? _____ (*times per week*)

THANK YOU FOR YOUR TIME!

APPENDIX 6: FOOD FREQUENCY QUESTIONNAIRE

Subject's Name:		Subject's Code:	
Food Frequency Questionnaire			
Investigators: Lindsey/ Wood/ Hegsted/ Mekary	Ochsner-LSU	Time Performed:	Date Performed:

Please put a tick (♦) on the appropriate answer:

I. VITAMINS

1. Have you ever regularly taken **multi-vitamins**?

✍ Never have

✍ Have in the past only

a) for how many years did you take them in the past?

☐ 1 year or less
 ☐ 2-4 years
 ☐ 5-9
 ☐ 10 or >

✍ Currently take them

a) how many per week?

b) how many years have you been taking them?

c) what brand do you usually use?

2. **Not counting multi-vitamins**, have you ever taken any one of the following specific vitamins or minerals?

Vitamin D

✍ Never taken

✍ Taken in the past only

✍ Yes, currently take it

Dose per day?

✍ less than 400 IU

✍ 400 to 600 IU

✍ 800 IU

✍ 801 IU or more

✍ Don't know

How long?

✍ 0-1 year

✍ 2-4 years

✍ 5-9 years

✍ ≥10 years

Calcium

✍ Never taken

✍ Taken in the past only

✍ Yes, currently take it

Dose per day?

✍ less than 400 mg

✍ 400 to 900 mg

✍ 901 to 1,300 mg

✍ 1,301 mg or more

✍ Don't know

How long?

✍ 0-1 year

✍ 2-4 years

✍ 5-9 years

✍ ≥10 years

Which **other supplements** are you currently taking on a regular basis (at least once per week)?

Please specify

II. Milk and milk products:

- a) Do you drink milk? 1. Yes _____ 2. No _____
- b) If yes, how many? _____ cups/week
- c) What kind? 1. Whole _____ 2. Skim _____ 3. Low fat _____
- d) Do you eat milk products? (e.g., yogurt, cream, ice cream, cheese, cream cheese, butter, etc....)
1. Yes _____ 2. No _____
- e) If yes, how much? _____ grams/week
- f) What kind? 1. Whole _____ 2. Skim _____ 3. Low fat _____

III. Eggs, Meat, and Fish:

- a) Do you consume meat or meat products? 1. Yes _____ 2. No _____
- b) If yes, how often per week? Answer by
1. Always 2. Sometimes 3. Rarely
- (Choose one for each)
1. Meat (Beef, pork, or lamb) _____
2. Chicken _____
3. Fish, shellfish, seafood _____
4. Eggs _____
5. Bacon _____
6. Turkey _____
7. Processed meat (Salami, bologna, or other) _____
- c) What kind of meat?
1. Lean _____ 2. Medium fat _____ 3. High fat _____

IV. Caffeine containing beverages

- a) Do you drink caffeine containing beverages? 1. Yes _____ 2. No _____
- b) If yes, how often per week? Answer by
1. Always 2. Sometimes 3. Rarely
- (Choose one for each)
1. Cola, Coke, Pepsi or Coke with caffeine _____
2. DIET Cola, Coke, Pepsi or Coke with caffeine _____
3. Tea with caffeine (not herbal) _____
4. Coffee with caffeine _____

V. Alcoholic beverages

- a) Do you drink alcoholic beverages? 1. Yes _____ 2. No _____
- b) If yes, how often per week? Answer by
1. Always 2. Sometimes 3. Rarely
- (Choose one for each)
1. Beer, regular _____
2. Beer, light _____
3. Red wine _____
4. Liquor, e.g. whiskey, gin, etc. _____

VI. Diet changes

a) Do you currently follow a special diet?

☐ No

☐ Yes

☐ physician prescribed ☐ Self prescribed

a) If yes, for how many years?

b) If yes, what kind of diet do you follow?

b) How has your use of the following foods and beverages changed over the past ten years? Please put a tick (♦) on the appropriate answer:

Food	Use has decreased	Use about the same	Use has increased
Whole Milk			
Skim milk			
Cheese			
Yogurt			
Butter			
Margarine			
Eggs			
Fish			
Red meat			
Tea			
Coffee			
Alcohol			

APPENDIX 7: SF36 HEALTH SURVEY

Subject's Name:		Subject's Code:	
SF36 Health Survey			
Investigators: Lindsey/ Wood/ Hegsted/ Mekary	Ochsner-LSU	Time Performed:	Date Performed:

INSTRUCTIONS: This set of questions asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities. Answer every question by marking the answer as indicated. If you are unsure about how to answer a question please give the best answer you can.

1. In general, would you say your health is: (Please tick **one** box.)

- Excellent
- Very Good
- Good
- Fair
- Poor

2. Compared to one year ago, how would you rate your health in general now? (Please tick **one** box.)

- Much better than one year ago
- Somewhat better now than one year ago
- About the same as one year ago
- Somewhat worse now than one year ago
- Much worse now than one year ago

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much? (**Please circle one number on each line.**)

Activities	Yes, limited a lot	Yes, limited a little	Not limited at all
3(a) Vigorous activities , such as running, lifting heavy objects, participating in strenuous sports	1	2	3
3(b) Moderate activities , such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	1	2	3
3(c) Lifting or carrying groceries	1	2	3
3(d) Climbing several flights of stairs	1	2	3
3(e) Climbing one flight of stairs	1	2	3
3(f) Bending, kneeling, or stooping	1	2	3
3(g) Walking more than a mile	1	2	3
3(h) Walking several blocks	1	2	3
3(i) Walking one block	1	2	3
3(j) Bathing or dressing yourself	1	2	3

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

(Please circle one number on each line.)

	Yes	No
4(a) Cut down on the amount of time you spent on work or other activities	1	2
4(b) Accomplished less than you would like	1	2
4(c) Were limited in the kind of work or other activities	1	2
4(d) Had difficulty performing the work or other activities (for example, it took extra effort)	1	2

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (e.g. feeling depressed or anxious)?

(Please circle one number on each line.)

	Yes	No
5(a) Cut down on the amount of time you spent on work or other activities	1	2
5(b) Accomplished less than you would like	1	2
5(c) Didn't do work or other activities as carefully as usual	1	2

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups? (Please tick **one** box.)

- Not at all
- Slightly
- Moderately
- Quite a bit
- Extremely

7. How much physical pain have you had during the past 4 weeks? (Please tick **one** box.)

- None
- Very mild
- Mild
- Moderate
- Severe
- Very Severe

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)? (Please tick **one** box.)

- Not at all
- A little bit
- Moderately
- Quite a bit
- Extremely

9. These questions are about how you feel and how things have been with you during the past 4 weeks. Please give the one answer that is closest to the way you have been feeling for each item.

(Please circle one number on each line.)	All of the time	Most of the time	A Good bit of the time	Some of the time	A little of the time	None of the time
9(a) Did you feel full of life?	1	2	3	4	5	6
9(b) Have you been a very nervous person?	1	2	3	4	5	6
9(c) Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
9(d) Have you felt calm and peaceful?	1	2	3	4	5	6
9(e) Did you have a lot of energy?	1	2	3	4	5	6
9(f) Have you felt downhearted and blue?	1	2	3	4	5	6
9(g) Did you feel worn out?	1	2	3	4	5	6
9(h) Have you been a happy person?	1	2	3	4	5	6
9(i) Did you feel tired?	1	2	3	4	5	6

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives etc.) (Please tick **one** box.)

- All of the time
- Most of the time
- Some of the time
- A little of the time
- None of the time

11. How TRUE or FALSE is each of the following statements for you?

(Please circle one number on each line)	Definitely True	Mostly True	Don't Know	Mostly False	Definitely False
11(a) I seem to get sick a little easier than other people	1	2	3	4	5
11(b) I am as healthy as anybody I know	1	2	3	4	5
11(c) I expect my health to get worse	1	2	3	4	5
11(d) My health is excellent	1	2	3	4	5

Thank You!

APPENDIX 8: HEALTH STATUS QUESTIONNAIRE

Subject's Name:		Subject's Code:	
HEALTH STATUS QUESTIONNAIRE			
Investigators: Lindsey/ Wood/ Hegsted/ Mekary	Ochsner-LSU	Time Performed:	Date Performed:

Prior to the start of any exercise program or testing a health fitness instructor must first administer to their client a Health Status Questionnaire. This tool will aid the personal trainer in deciding what course of action should be followed in regards to program recommendations.

Code For Health Status Questionnaire

EI = Emergency Information-must be made readily available.

MC = Medical Clearance needed-do not allow to exercise without physician's permission.

SEP = Special Emergency procedure needed-do not let participant exercise alone; make sure the person's exercise partner knows what to do in case of emergency.

RF = Risk factor for CHD (educational materials and workshops needed)

SLA = Special or Limited activities may be needed-you may want to include or exclude specific exercises.

OTHER (not marked) = Personal information that may be helpful for files or research.

Instructions

Complete each question as accurately as possible. All information is confidential.

Part 1. General information

1. Name _____ Nickname _____

2. Mailing Address _____ Phone (H) _____

_____ Phone (W) _____

3. *EI* Personal Physician _____ Phone _____

Physician Address _____

4. *EI* Person to contact in case of emergency _____ Phone _____

5. Gender (circle one): Female Male *RF*

6. *RF* Date of birth _____ / _____ / _____

7. Number of hours worked per week: Less than 20 20-40 41-60 over 60

8. *SLA* More than 25% of the time at your job is spent (circle all that apply)

Sitting at desk Lifting loads Standing Walking Driving

Part 2. Medical History

10. *RF* Circle any who died of heart attack before age 50:

Father Mother Brother Sister Grandparent

11. Date of

Last medical physical exam: _____

Last physical fitness test: _____

12. Circle any operations that you have had:

Back *SLA* Heart *MC* Kidney *SLA* Eyes *SLA* Joint *SLA* Neck *SLA*
Ears *SLA* Hernia *SLA* Lung *SLA* Other _____

13. Circle all medicine taken in last 6 months:

Blood thinner *MC* Epilepsy medication *SEP* Nitroglycerin *MC*
Diabetic *SEP* Heart rhythm medication *MC* Other _____
Digitalis *MC* High blood pressure medication *MC*
Diuretic *MC* Insulin *MC*

14. Please circle any of the following for which you have been diagnosed or treated by a physician or health professional:

Alcoholism <i>SEP</i>	Diabetes <i>SEP</i>	Kidney problem <i>MC</i>
Anemia, sickle cell <i>SEP</i>	Emphysema <i>SEP</i>	Mental illness <i>SEP</i>
Anemia, other <i>SEP</i>	Epilepsy <i>SEP</i>	Neck strain <i>SLA</i>
Asthma <i>SEP</i>	Eye problems <i>SLA</i>	Obesity <i>RF</i>
Back strain <i>SLA</i>	Gout <i>SLA</i>	Phlebitis <i>MC</i>
Bleeding trait <i>SEP</i>	Hearing loss <i>SLA</i>	Rheumatoid arthritis <i>SL</i>
Bronchitis, chronic <i>SEP</i>	Heart problems <i>MC</i>	Stroke <i>MC</i>
Cancer <i>SEP</i>	High blood pressure <i>RF</i>	Thyroid problem <i>SEP</i>
Cirrhosis <i>MC</i>	HIV <i>SEP</i>	Ulcer <i>SEP</i>
Concussion <i>MC</i>	Hypoglycemia <i>SEP</i>	Other _____
Congenital defect <i>SEP</i>	Hyperlipidemia <i>RF</i>	

15. Any of these health symptoms that occurs frequently requires medical attention. Circle the number indicating how often you have each of the following:

5= Very often

4= Fairly often

3= Sometimes

2= Infrequently

1= Practically never

a. Cough up blood *MC*

1 2 3 4 5

b. Abdominal pain *MC*

1 2 3 4 5

c. Low-back pain *MC*

1 2 3 4 5

d. Leg Pain *MC*

1 2 3 4 5

e. Arm or shoulder pain *MC*

1 2 3 4 5

f. Chest pain *RF MC*

1 2 3 4 5

g. Swollen joints *MC*

1 2 3 4 5

h. Feel faint *MC*

1 2 3 4 5

i. Dizziness *MC*

1 2 3 4 5

j. Breathlessness with slight exertion *MC*

1 2 3 4 5

k. Palpitation or fast heart beat *MC*

1 2 3 4 5

l. Unusual fatigue with normal activity *MC*

1 2 3 4 5

Part 3. Health-related behaviors

16. *RF* Do you now smoke? Yes No
17. *RF* If you are a smoker, indicate the number smoked per day:
- | | | | |
|------------------------------------------------|-------|-------|-------------|
| Cigarettes: 40 or more | 20-39 | 10-19 | 1-9 |
| Cigars or pipes only: 5 or more or any inhaled | | | less than 5 |
18. *RF* Do you exercise regularly? Yes No
19. How many days a week do you accumulate 30 minutes of moderate activity?
- | | | | | | | | | |
|---|---|---|---|---|---|---|---|---------------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | days per week |
|---|---|---|---|---|---|---|---|---------------|
20. How many days per week do you normally spend at least 20 minutes in vigorous exercise?
- | | | | | | | | | |
|---|---|---|---|---|---|---|---|---------------|
| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | days per week |
|---|---|---|---|---|---|---|---|---------------|
21. Can you walk 4 miles briskly without fatigue? Yes No
22. Can you jog 3 miles at a moderate pace without discomfort? Yes No
23. Weight now: _____ lb. One year ago: _____ Age 21: _____

Part 4. Health-related attitudes

24. These are traits that have been associated with coronary-prone behavior. Circle the number that corresponds to how you feel towards the following statement:
- I am an impatient , time-conscious, hard-driving individual.

Circle the number that best describes how you feel:

- | | |
|----|---------------------|
| 6= | strongly agree |
| 5= | Moderately agree |
| 4= | Slightly agree |
| 3= | Slightly disagree |
| 2= | Moderately disagree |
| 1= | Strongly disagree |

25. List everything not included on this questionnaire that may cause you problems in a fitness test or fitness program:

THANK YOU FOR YOUR TIME!

Description of the study

- During Visit One the following measurements will be obtained:

A. Physical Activity Questionnaire (30 minutes)

You will be asked to complete the Aerobic Center Longitudinal Study Physical Activity Questionnaire. This questionnaire will be used to measure physical activity patterns, including leisure and household, during the past 3 months.

B. Physical Activity Readiness questionnaire (PAR-Q) (10 minutes)

You will be asked to complete the Physical Activity Readiness questionnaire (PAR-Q). This questionnaire will be used to determine if you will need to see a physician before beginning this exercise program.

C. Food Frequency Questionnaire (15 minutes)

You will be asked to complete this questionnaire to identify past dietary patterns and look at use of calcium/vitamin D intake, including supplements, and calcium rich food, as well as high-protein foods, caffeine containing beverages, and alcoholic beverages.

D. Short Form 36 (20 minutes)

You will be asked to complete the Short Form 36. This questionnaire is designed to assess your strength, any pain you might have with activity, and your general well-being.

E. Health Status Questionnaire (10 minutes)

You will be asked to complete the Health Status Questionnaire. This questionnaire is designed to assess medical history and health related behaviors.

F. Dual Energy Xray Absorptiometry (DXA)

DXA scan measurements for lower back will be used at the end of the study.

- During Visit Two, you will be asked to perform a fitness test.

A. Isometric strength

Isometric strength of back extensor muscles will be measured using a back isometric dynamometer (Biodex) at baseline, 6 months, and one year.

Following the completion of the initial visits and upon selection of the n pairs, women randomly assigned to the treatment group (n/2) will be taught the core/lower back strengthening. The Thera-Band® Exercise Ball will be introduced to the women and gradually incorporated into the exercise regimen for the core and lower back. These exercises will be described in the following paragraph. Some other movements will be used from Sara Meek's book, who is a physical therapist who treats osteoporosis. You will have to perform these exercises for a period of 1 year, 3 times a week, 40-45 minutes each time. The women assigned to the control group will be asked to maintain the same pattern of their dietary intake and physical activity throughout the study and will be asked to attend the three meetings for measurements of lower back strength.

Exercise description

i. Warm-up: (5 minutes).

A thorough warm-up preparing the back for the exercises to come is completed at first

ii. Strengthening

To strengthen the back muscles, 30 minutes of the following core/lower back exercises should be done 3 times a week.

iiia. Abdominal Exercises (core exercises)

1-Pelvic lift: Lie on the floor supine position with knees bent, feet shoulder-width apart, and arms to the side; tighten the abdominal muscles, lift the pelvis slightly off the ground without bouncing, and without using buttocks or leg muscles; hold for 5 seconds and slowly release the pelvis back down on the floor. After 3 months of exercising, perform the same movement on the Thera-Band Exercise Balls c, where you put your feet/heels on the ball instead of the floor. Do 2 sets of 15

2-Core strengthening: Lie on the floor supine position with knees bent, feet shoulder-width apart. Grab both knees and press them against the chest. Extend one leg out and take it slowly down towards the floor, without letting it touch the floor. The leg should stop from going down at the level when then lower back starts to arch. Once at that level, take your leg back in and repeat with the other leg. Do 2 sets of 10.

3- Standing knee lifts: Stand with right hand holding on to side of chair; raise left knee slowly to 90 degree angle; grab behind left knee with left hand and slowly bring the knee up to the chest; hold it for 5 seconds, keeping the core inwards and exhaling, then lower slowly to the starting position, inhaling. Repeat the same with the other leg. Do 2 times 15 for each leg.

4-Standing leg adduction: Stand with right hand holding on to side of chair. Raise one straight leg slowly to the side keeping the core contracted inwards; exhale, then lower slowly to the starting position, inhaling. Repeat the same with the other leg. Do 2 times 15 for each leg.
PS: Exercises 3 and 4 can be combined together in one exercise where the leg goes from forward bent 90 degrees position to side extended position.

5-Arm/Leg raises: Get down on your hands and knees and keep your core inwards and back in a neutral straight position (cat position); keeping your neck and back straight; slowly lift your right arm and the left leg to make one straight line parallel to the floor along with the back. Your head should be looking towards the floor keeping the neck in a neutral position. Exhale as you reach out and keep the core inwards. Slowly go back to starting position and repeat the same routine with the other arm and its opposite leg. Do 4 sets of 10

iiib. Back Exercises collated from (Hyde, 2001) with some modifications done by the investigator (R.M.).

1-Prone arm/leg exercises: Lie on stomach –prone position, face-down keeping neck straight with legs straight and arms straight overhead; Slowly lift the right arm along with the left leg, hold for 2 seconds and come down. Repeat with left arm and right leg. Do 4 sets of 10. If the participant fails to accomplish this exercise, he/she can start gradually with lifting each arm alone at first, then each leg, then combining both leg and arm.

2-Back extension: Keep the previous position. Repeat lifting the torso slowly off the ground while keeping the legs on the floor, with both arms behind the head and return to start position (10 times). For a harder exercise, repeat stretching the arms out like a cross (10 times), and then stretching the arms forward (10 times). The last advanced exercise can be given in one month from the day of the study.

3- Cat curls: Get down on your hands and knees and keep your core inwards and back in a neutral straight position. Your head should be facing the floor. Curve your back inwards making a C shape towards the floor; rise your head looking upwards while inhaling; hold for 3 seconds; then curve your back outwards in a mountain shape while exhaling; your head should be looking downwards; hold for 3 seconds; go back to neutral position. Do 2 sets of 10.

4-Back stretches: Lie in prone position, lifting the torso up leaning on the elbows. Hold for 10 seconds. Move backward on the bent knees, stretching the arms forward, pulling head between arms. Let your gluteus touch your heels. Hold for 10 seconds. Gently stand on the feet while keeping the torso down; cross the arms and grab behind the knees with the palms. Very gently arch the back upwards to the ceiling (C shape in the back), while grabbing behind the knees with the palms. Hold for 10 seconds. Gently roll the back all the way up. Repeat the final stretch exercise 5 times.

RISKS

The risks associated with low-to-moderate physical exertion are extremely low, even among persons with cardiovascular disease. However, there are remote risks of muscle strains, and other bone and joint discomforts, as well as remote risks of heart attack, stroke, and death. You might be subject to lose balance and fall when using the stability ball but this is rare if proper teaching technique is used. You should also know that your condition of osteopenia may not improve or may worsen, despite participation. In the general population it would be expected that 1 in every 2.2 million tests would result in some heart complication requiring medical attention, and roughly 1 in every 3 million tests would result in death.

Louisiana state law requires that participants in all clinical studies such as this one be informed that any study (or procedure) may also result in death, brain damage, quadriplegia (paralysis in all arms and legs), paraplegia (paralysis of both legs), loss of organ, loss of arm or leg, loss of function of organ, loss of function of an arm or leg, and disfiguring scars.

BENEFITS

Women with low bone density need special care and specific types of practical exercises that they can adhere and follow. The idea of finding some convenient, safe, and beneficial exercises for the elderly women who cannot lift any weights and who cannot go to the gym is very crucial in adding a practical help in the life of these aged women. This research will further determine whether specific strength exercise for the core and lower back with no external load and with more frequency have a positive effect on the lumbar mineral density and on the extensor back muscles' strength. Not only the study may benefit the participant directly, but it may also benefit

others by providing information regarding the optimal type, intensity, and duration of exercise that may elicit lumbar mineral density.

Regular physical exercise is shown to improve heart and blood vessel function, muscle strength and endurance, and bone health. Further, exercise is known to reduce the risk of serious diseases such as heart disease, osteoporosis, type II diabetes, and some cancers. Lastly, regular exercise has also been linked to improved mood and sense of well-being.

However, no promise can be made concerning the study outcome, because results from a clinical research study cannot be predicted. Your physician, and those involved in this research study, will take every precaution consistent with the best medical practice.

COSTS

In case of inadequate calcium intake, you will be given free calcium supplementation. The fitness assessment, the muscle strength measurement, the muscle endurance measurement, and the training will be under no costs. No other additional costs will be involved.

PAYMENT FOR PARTICIPATION AND/OR REIMBURSEMENT OF EXPENSES

Payment for participation or reimbursement of expenses will not be provided.

COMPENSATION FOR INJURY

If there is an injury due to the research procedures, medical treatment, if necessary for injuries or illness, is available. This medical treatment and/or hospitalization is not free of charge. If you think you have an injury that may be related to the research procedures, you should call Dr. Stephen Lindsey at (225) 761 5868 or Dr Robert Wood at Louisiana State University at 225/578-9142

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study doctor must get your authorization (permission) to use or give out any health information that might identify you.

What information may be used and given to others?

If you choose to be in this study, the study doctor will get personal information about you. This may include information that might identify you. The study doctor may also get information about your health including:

- Medical and research records
- Records about phone calls

- Records about your study visits
- Records of physical exams
- Laboratory, x-ray, DEXA scans, and other test results
- Diaries and questionnaires
- Records about your calcium and vitamin D status

Who may use and give out information about you?

Information about your health may be used and given to others by the study doctor and staff. They might see the research information during and after the study.

Who might get this information?

Information about you and your health which might identify you may be given to:

- Ochsner Clinic Foundation Institutional Review Board (IRB)
- Ochsner Clinic Foundation Research & Compliance Offices
- Louisiana State University Institutional Review Board (IRB)

Why will this information be used and/or given to others?

Information about you and your health that might identify you may be given to others to carry out the research study.

The results of this research may be published in scientific journals or presented at scientific meetings, but your identity will not be disclosed.

The Ochsner IRB may review the information. The IRB is a group of people who perform independent review of research as required by regulations. The Ochsner Research & Compliance Offices may review this research in their oversight and auditing roles.

What if I decide not to give permission to use and give out my health information?

By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. If you refuse to give permission, you will not be able to be in this research.

May I review or copy the information obtained from me or created about me?

You have the right to review and copy your health information. However, if you decide to be in this study and sign this permission form, you will not be allowed to look at or copy your information until after the research is completed.

May I withdraw or revoke (cancel) my permission?

This permission will not stop automatically.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to continue being in this study.

When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Is my health information protected after it has been given to others?

If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others without your permission. Your personal information may be disclosed if required by law.

QUESTIONS

If you have any questions concerning your participation in this study, or if at any time you feel you have experienced a research-related injury or a reaction to a study drug, contact:

Dr. Stephen Lindsey at Ochsner Clinic
Address: 9001 Summa Avenue, Baton Rouge, LA

Phone: 225-761 5868

If you have questions about your rights as a research subject, you may contact:

Ochsner Clinic Foundation Institutional Review Board (OCF IRB)
1514 Jefferson Highway, Brent House 514
New Orleans, LA 70121
Telephone: 1-504-842-3535

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

If you agree to participate in this study, you will receive a signed and dated copy of this consent form for your records.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

Participation in this study is voluntary. You may decide not to participate in this study or you may withdraw from this study at any time without penalty or loss of benefits to which you are otherwise entitled at this site. You will be informed of any significant new findings that develop during the investigation that may affect your willingness to continue in the study.

You should tell your study doctor about all of your past and present health conditions and allergies of which you are aware, and all drugs and medications which you are presently using.

Your participation in this study may be stopped at any time by the study doctor without your consent because:

- the study doctor thinks it necessary for your health or safety;
- you have not followed study instructions;
- administrative reasons require your withdrawal.

If you leave the study before the final regularly scheduled visit, you may be asked by the study doctor to make a final visit for some end of study procedures.

CONSENT

I have read the information in this consent form (or it has been read to me). All my questions about the study and my participation in it have been answered. I freely consent to participate in this research study. I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above. By signing this consent form I have not waived any of the legal rights which I otherwise would have as a subject in a research study.

CONSENT SIGNATURE

Patient Signature

Printed Name

Date

Person Obtaining Consent - Signature

Printed Name

Date

----- Use the following only if applicable -----

If this consent form is read to the subject because the subject (or legally authorized representative) is unable to read the form, an impartial witness must be present for the consent and sign the following statement:

I confirm that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject (or the subject's legally authorized representative). The subject (or the subject's legally authorized representative) freely consented to participate in the research study.

Signature of Impartial Witness	Printed Name	Date
--------------------------------	--------------	------

Note: This signature block cannot be used for translations into another language. A translated consent form, with the translation approved by the IRB, is necessary for enrolling subjects who do not speak English.

THANK YOU FOR YOUR TIME!

APPENDIX 10: CORE LOWER BACK STRENGTHENING EXERCISES

A thorough warm-up preparing the back for the exercises to come is completed for the first five minutes. To strengthen the back muscles, 30-40 minutes of the following core/lower back exercises should be done 3 times a week.

CORE EXERCISES

1-Pelvic Lift: Lie on the floor supine position with knees bent, feet shoulder-width apart, and arms to the side; tighten the abdominal muscles, lift the pelvis slightly off the ground without bouncing, and without using buttocks or leg muscles; hold for 5 seconds, exhale, then slowly release the pelvis back down on the floor. After three months of exercising, perform the same movement on the Thera-Band Exercise Balls, where you put your feet/heels on the ball instead of the floor. Do 2 sets of 15



2-Core Strengthening: Lie on the floor supine position with knees bent, feet shoulder-width apart. Grab both knees and press them against the chest. Extend one leg out while exhaling and take it slowly down towards the floor, without letting it touch the floor. The leg should stop from going down at the level when then lower back starts to arch. Once at that level, take your leg back in and repeat with the other leg. Do 2 sets of 10



3- Standing Knee Lifts: Stand with right hand holding on to side of chair; raise left knee slowly to 90 degree angle; grab behind left knee with left hand and slowly bring the knee up to the chest; hold it for 5 seconds, keeping the core inwards and exhaling, then lower slowly to the starting position, inhaling. Repeat the same with the other leg. Do 2 times 15 for each leg.



4-Standing Leg Adduction: Stand with right hand holding on to side of chair. Raise one straight leg slowly to the side keeping the core contracted inwards; exhale, then lower slowly to the starting position, inhaling. Repeat the same with the other leg. Do 2 times 15 for each leg.



PS: Exercises 3 and 4 can be combined together in one exercise where the leg goes from forward bent 90 degrees position to side extended position

5-Arm/Leg Raises: Get down on your hands and knees and keep your core inwards and back in a neutral straight position (cat position); keeping your neck and back straight; slowly lift your right arm and the left leg to make one straight line parallel to the floor along with the back. Your head should be looking towards the floor keeping the neck in a neutral position. Exhale as you reach out and keep the core inwards. Slowly go back to starting position and repeat the same routine with the other arm and its opposite leg. Do 4 sets of 10



BACK EXERCISES collated from (Hyde, 2001) with some modifications done by the investigator (R.M.)

1-Prone Arm/Leg Exercises: Lie on stomach –prone position, face-down keeping neck straight with legs straight and arms straight overhead; Slowly lift the right arm along with the left leg, exhale, hold for 2 seconds and come down. Repeat with left arm and right leg. Do 4 sets of 10. If the participant fails to accomplish this exercise, he/she can start gradually with lifting each arm alone at first, then each leg, then combining both leg and arm.



2-Back Extension: Keep the previous position. Repeat lifting the torso slowly off the ground while keeping the legs on the floor and exhaling, with both arms behind the head and return to start position (10 times). For a harder exercise, repeat stretching the arms out like a cross (10 times), and then stretching the arms forward (10 times). The last advanced exercise can be given in one month from the day of the study.



3- Cat Curls: Get down on your hands and knees and keep your core inwards and back in a neutral straight position. Your head should be facing the floor. Curve your back inwards making a C shape towards the floor; rise your head looking upwards while inhaling; hold for 3 seconds; then curve your back outwards in a mountain shape while exhaling; your head should be looking downwards; hold for 3 seconds; go back to neutral position. Do 2 sets of 10.



4-Back Stretches: Lie in prone position, lifting the torso up leaning on the elbows. Hold for 10 seconds. Move backward on the bent knees, stretching the arms forward, pulling head between arms. Let your gluteus touch your heels. Hold for 10 seconds. Gently stand on the feet while keeping the torso down; cross the arms and grab behind the knees with the palms. Very gently arch the back upwards to the ceiling (C shape in the back), while grabbing behind the knees with the palms. Hold for 10 seconds. Gently roll the back all the way up. Repeat the final stretch exercise 5 times.



THANK YOU FOR YOUR TIME TO COMPLETE THE EXERCISES!

Pictures performed by the investigator Rania Mekary.

VITA

Born in a small village in Northern Lebanon (Gabriel/Akkar) in 1973, Rania A. Mekary attended a private catholic school in Tripoli not very far from the village, where she earned her Lebanese and French Baccalaureate diplomas in 1990. Then, Rania traveled to Paris, France where she studied two years of medical science in Paris V University. Upon her return to Lebanon, she earned both her bachelor's and master's degrees in nutrition in 1995 and 1998 respectively, both from the American University of Beirut. She later worked for two and a half years as a "Professional Nutritionist" at the Ministry of Agriculture in Beirut (Lebanon) until August 2001. To fulfill her dreams and further her education, Rania pursued her doctoral studies attending the Louisiana State University in Baton Rouge. Member of the Gamma Beta Phi Society (2002) and of the Gamma Sigma Delta (2004) honor societies, she earned two minors in kinesiology and epidemiology in 2005, a master's in statistics in May 2005, and has just successfully defended her dissertation on June 17, 2005. Rania is expecting to earn her doctoral degree in August 2005, after which she will go for a 2-3 years postdoctoral fellowship in 'Nutrition and Cancer Epidemiology' at the School of Public Health at Harvard, in Boston, Massachusetts on September 1st, 2005. Some of Rania's hobbies are physical activity and group exercise teaching. Rania has been training different classes since 1995. She is a certified "Body Training System" Aerobics instructor. Ultimately, Rania's dreams are to make a positive contribution in the world of nutrition.